Incomplete Systemic Recovery and Metabolic Phenoreversion in Post-Acute Phase Non-Hospitalized COVID-19 Patients: Implications for Assessment of Post Acute COVID-19 Syndrome

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  - Demographic information about the population of the recovery cohort
- Targeted MS
  - Univariate statistics
  - Correlation Matrices

- Lipoproteins measured by IVDR method
  - Univariate statistics
  - Correlation matrix

- Small molecules measured by IVDR method
  - Univariate statistics

- Diffusion and Relaxation edited NMR experiments
  - Univariate statistics

Contents

Table S1: list of parameters considered from targeted MS assays

	metabolite	Phenoreversion status
1	3-hydroxykynurenine	Normalized
2	3-hydroxykynurenine/kynurenic acid	Normalized
3	aspartic acid	Substantially normalized
4	citrulline	Normalized
5	Fisher's ratio	Normalized
6	glutamic acid	Substantially normalized
7	glutamine/glutamic acid	Substantially not normalized
8	histidine	Normalized
9	indole-3-acetic acid	Substantially normalized
10	kynurenine	Partially normalized
11	kynurenine/tryptophan	Substantially normalized
12	neopterin	Normalized
13	phenylalanine	Normalized
14	phenylalanine/tyrosine	Normalized
15	quinolinic acid	Normalized
16	quinolinic acid/kynurenic acid	Normalized
17	taurine	Substantially not normalized
18	tryptophan	Substantially normalized

Table S2: list of parameters considered from IVDr Lipoproteins

	metabolite	Class/ subclass	Compound	Concentration unit	Phenoreversion status
22	ABA1	Ratio of Apolipoproteins A1 and B100	Apolipoprotein-A1 / Apolipoprotein-B100	-/-	Normalized
23	H1FC	HDL-1 Subclass	Free Cholesterol	mg/dL	Normalized
24	H2A1	HDL-2 Subclass	Apolipoprotein-A1	mg/dL	Normalized
25	H2FC	VLDL-2 Subclass	Free Cholesterol	mg/dL	Normalized
26	H3A1	HDL_3 subclass	Apolipoprotein-A1	mg/dL	Normalized
27	H3CH	HDL-3 Subclass	Cholesterol	mg/dL	Normalized
28	H3FC	HDL-3 Subclass	Free Cholesterol	mg/dL	Normalized
29	H3PL	HDL-3 Subclass	Phospholipids	mg/dL	Normalized
30	H4A1	HDL-4 Subclass	Apolipoprotein-A1	mg/dL	Partially normalized
31	H4A2	HDL-4 Subclass	Apolipoprotein-A2	mg/dL	Partially normalized
32	H4CH	HDL-4 Subclass	Cholesterol	mg/dL	Substantially normalized
33	H4FC	HDL-4 Subclass	Free Cholesterol	mg/dL	Normalized
34	H4PL	HDL-4 Subclass	Phospholipids	mg/dL	Normalized
35	HDA1	HDL Class	Apolipoprotein-A1	mg/dL	Substantially normalized
36	HDA2	HDL Class	Apolipoprotein-A2	mg/dL	Normalized
37	HDCH	HDL Class	Cholesterol	mg/dL	Normalized
38	HDFC	HDL Class	Free Cholesterol	mg/dL	Normalized
39	HDPL	HDL Class	Phospholipids	mg/dL	Normalized
40	IDAB	IDL Class	Apolipoprotein_B100	mg/dL	Normalized
41	IDPN	IDL	Particle Number	nmol/L	Normalized
42	L2TG	LDL-2 Subclass	Triglycerides	mg/dL	Normalized
43	L4TG	LDL-4 Subclass	Triglycerides	mg/dL	Normalized
44	L5TG	LDL-5 Subclass	Triglycerides	mg/dL	Normalized
45	LDHD	Ratio LDL and HDL Cholesterol	LDL Cholesterol / HDL Cholesterol	-/-	Normalized
46	LDTG	LDL Class	Triglycerides	mg/dL	Normalized
47	TPA1	Total Plasma	Apolipoprotein-A1	mg/dL	Normalized
48	TPA2	Total Plasma	Apolipoprotein-A2	mg/dL	Substantially normalized
49	TPCH	Total Plasma	Cholesterol	mg/dL	Substantially

50	V4FC	VLDL-4 Subclass	Free Cholesterol	mg/dL	normalized Normalized

Table S3: list of parameters considered from IVDr small molecules

	metabolite	**Phenoreversion status**
54	Glucose	Normalized

Table S4: list of parameters considered from DIRE NMR experiments

	metabolite	***Phenoreversion status***
55	GlycA	Substantially normalized
56	GlycB	Substantially normalized
57	Spc Total	Normalized
58	Spc Total / GlycA	Substantially normalized

Demographic information about the population of the recovery cohort

Table S5: Demographic information about the population of the recovery cohort

patientID	class	Gender	Age	BMI	BMI1
COV01078	positive_recovery	Female	52	25.7	25.7
COV01054	positive_recovery	Male	28	24.4	24.1
COV01043	positive_recovery	Male	65	25.2	24.6
COV01059	positive_recovery	Female	54	24.0	23.7
COV01046	positive_recovery	Male	66	44.7	40.8
COV01075	positive_recovery	Female	71	31.6	34.6
COV01091	positive_recovery	Male	72	29.6	29.6
COV01029	positive_recovery	Female	21	22.0	20.7
COV01061	positive_recovery	Male	61	25.8	26.4
COV01045	positive_recovery	Male	67	25.4	25.0
COV01012	positive_recovery	Male	33	27.51	26.9
COV01090	positive_recovery	Female	50	NA	NA
COV01027	positive_recovery	Female	61	25.3	26.7
COV01034	positive_recovery	Female	59	50.8	47.0
COV01050	positive_recovery	Male	59	26.8	26.2
COV01025	positive_recovery	Female	20	21.9	21.5
COV01076	positive_recovery	Female	71	23.9	25.0
COV01005	positive_recovery	Female	68	26.4	26.4
COV01084	positive_recovery	Female	32	28.3	31.6
COV01013	positive_recovery	Male	56	31.6	30.7
COV01007	positive_recovery	Male	63	27.5	26.1
COV01044	positive_recovery	Female	80	27.5	36.6
COV01014	positive_recovery	Female	55	25.7	27.5
COV01030	positive_recovery	Female	64	35.0	39.1
COV01069	positive_recovery	Female	56	37.1	37.1
COV01085	positive_recovery	Male	62	30.3	31.3
COV01041	positive_recovery	Female	53	34.9	29.4
COV01003	positive_recovery	Male	30	24.3	24.3
COV01002	positive_recovery	Female	72	29.8	33.2
COV01026	positive_recovery	Male	81	30.2	32.6
COV01057	positive_recovery	Female	51	24.8	24.8

COV01081	positive_recovery	Female	57	27.8	26.6
COV01074	positive_recovery	Male	69	26.1	NA
COV01172	positive_recovery	Male	64	25.3	22.9

Table S6. Description of the number of samples(patients) included in each method.

Methods Patient Group	Targeted MS	Lipoproteins (NMR)	NMR IVDR/ DIRE (integrals)
Healthy Controls	28 (28)	43 (41)	34 (34)
SARS-CoV-2 Positive (+)	17 (10)	68 (17)	57 (18)
Follow-up	27 (27)	27 (27)	31 (27)

Targeted MS

Univariate statistics

Figure S1: 3-hydroxykynurenine

targeted MS / pos[17], hty[28], rec[27], total [72]

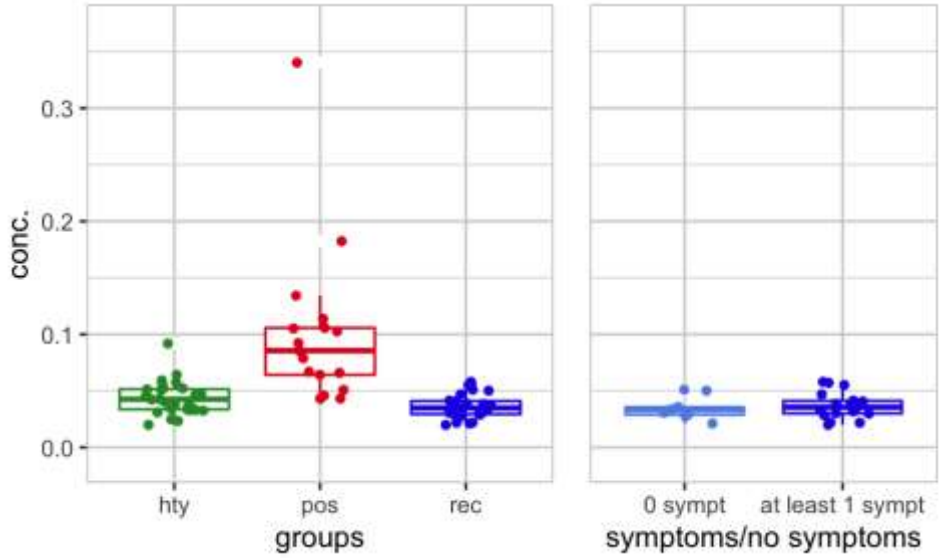


Figure S2: 3-hydroxykynurenine/kynurenic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

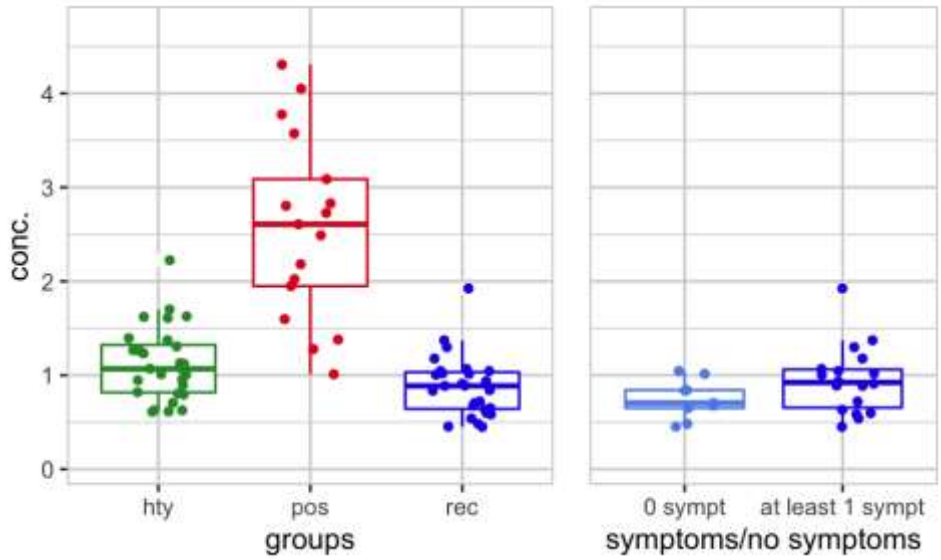


Figure S3: aspartic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

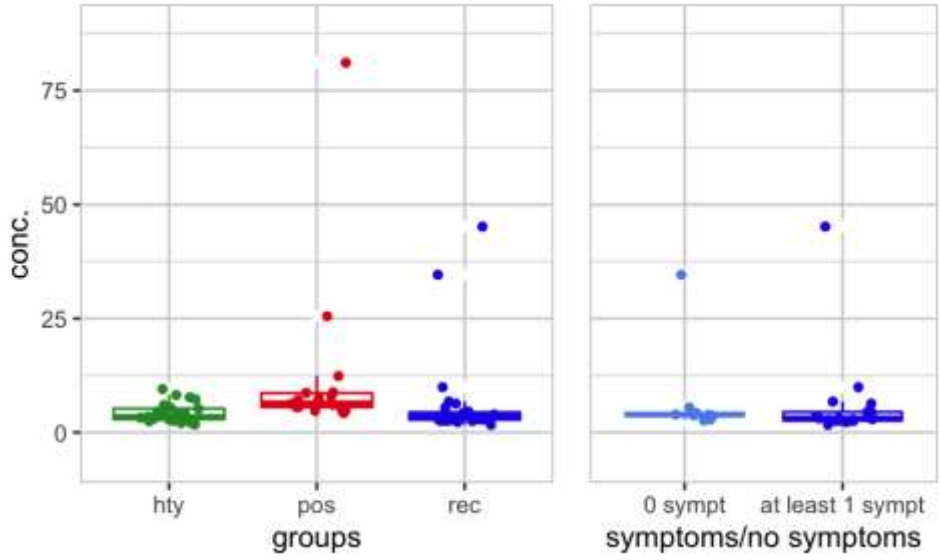


Figure S4: citrulline

targeted MS / pos[17], hty[28], rec[27], total [72]

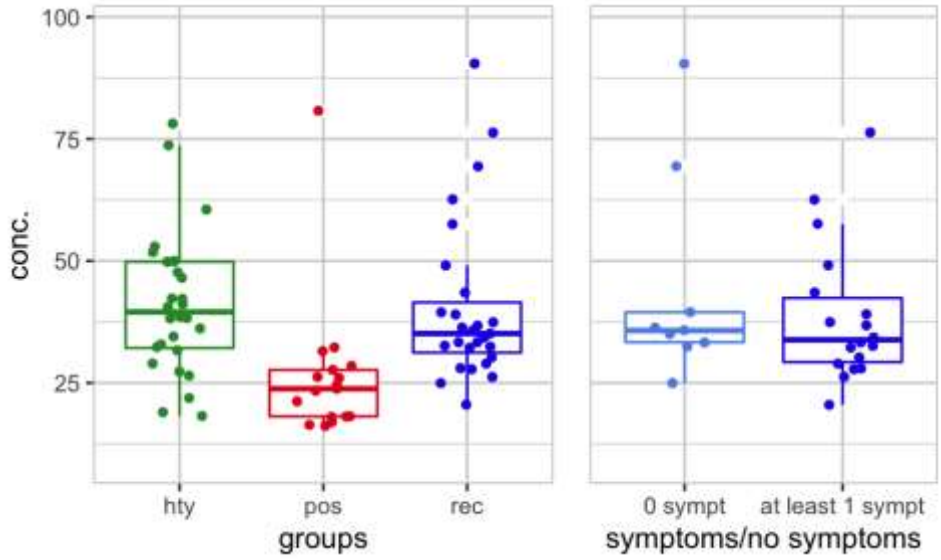


Figure S5: Fisher's ratio

targeted MS / pos[17], hty[28], rec[27], total [72]

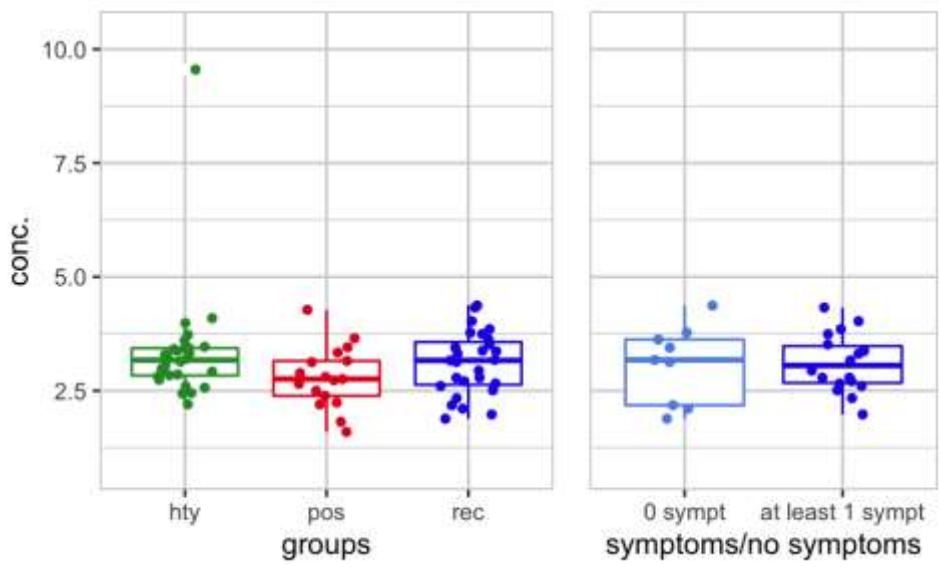


Figure S6: glutamic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

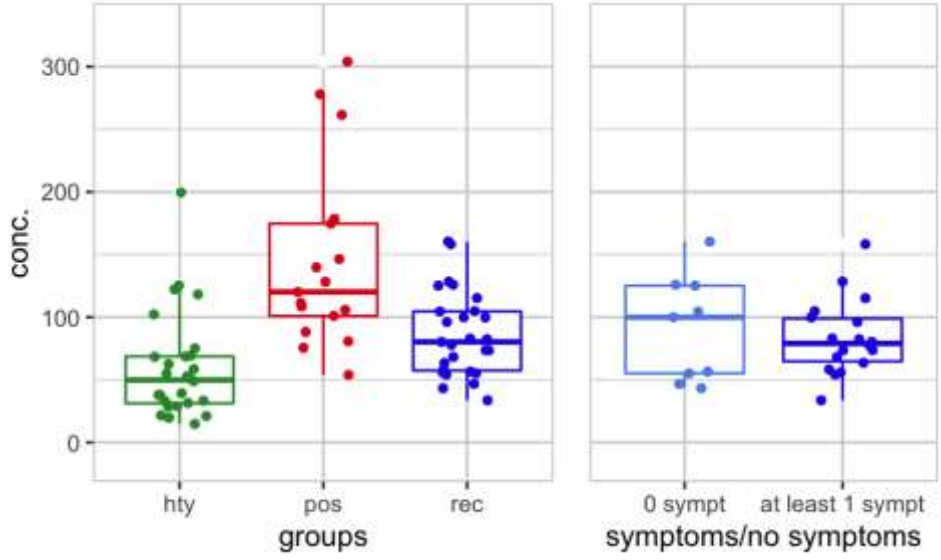


Figure S7: glutamine/glutamic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

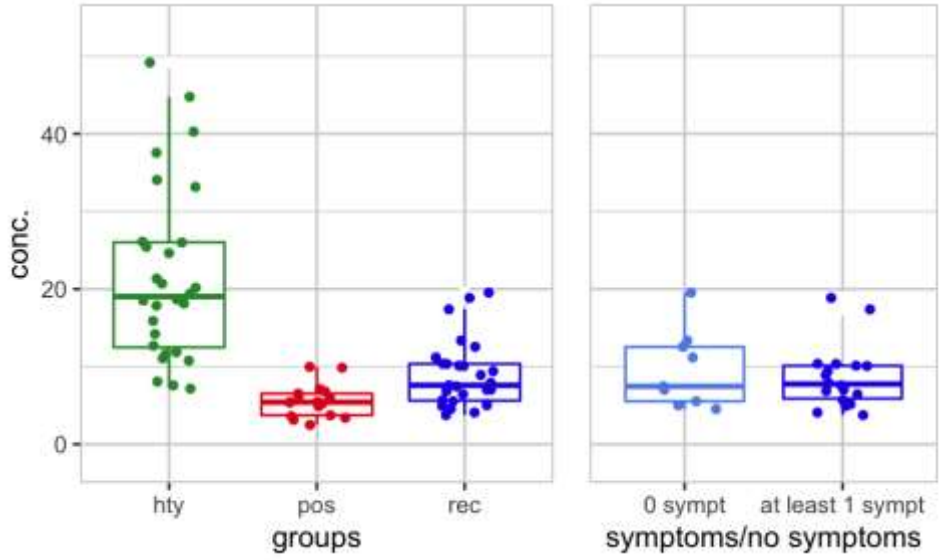


Figure S8: histidine

targeted MS / pos[17], hty[28], rec[27], total [72]

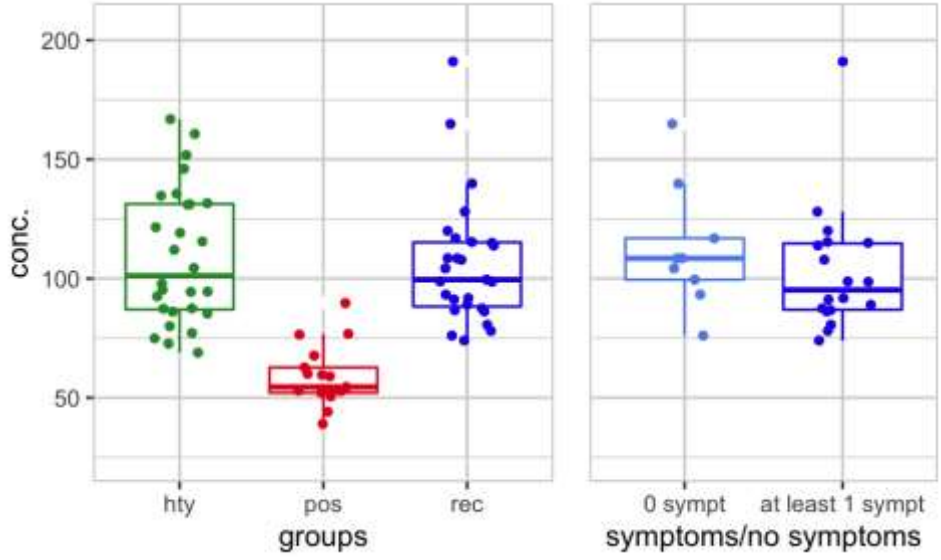


Figure S9: indole-3-acetic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

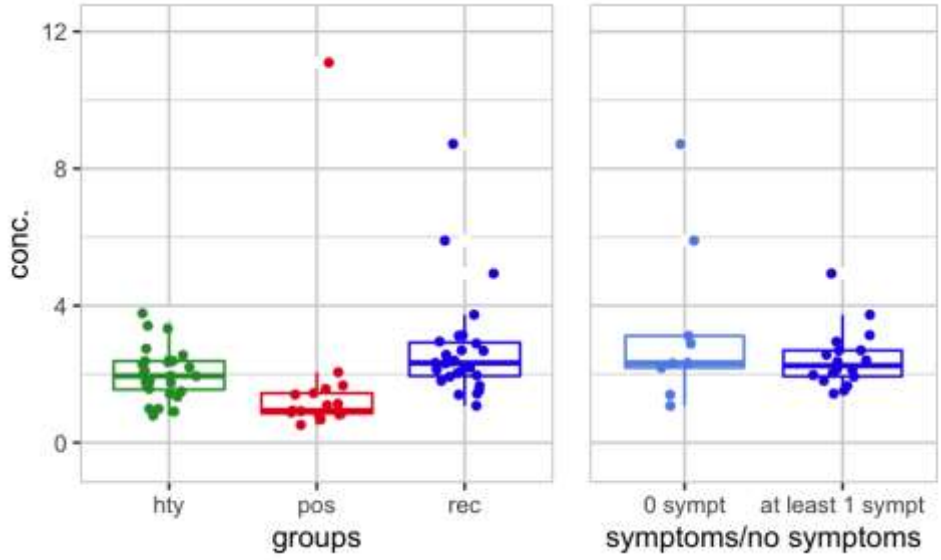


Figure S10: kynurenine

targeted MS / pos[17], hty[28], rec[27], total [72]

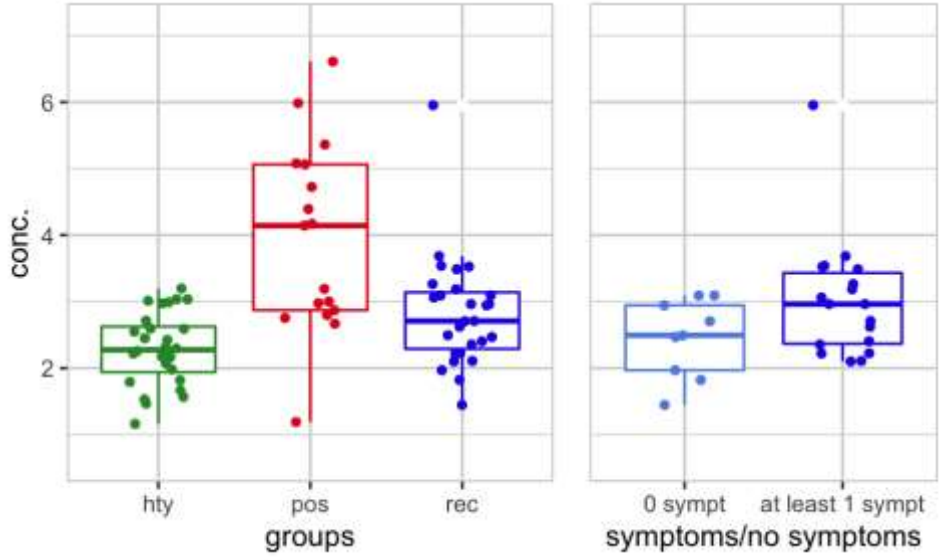


Figure S11: kynurenine/tryptophan

targeted MS / pos[17], hty[28], rec[27], total [72]

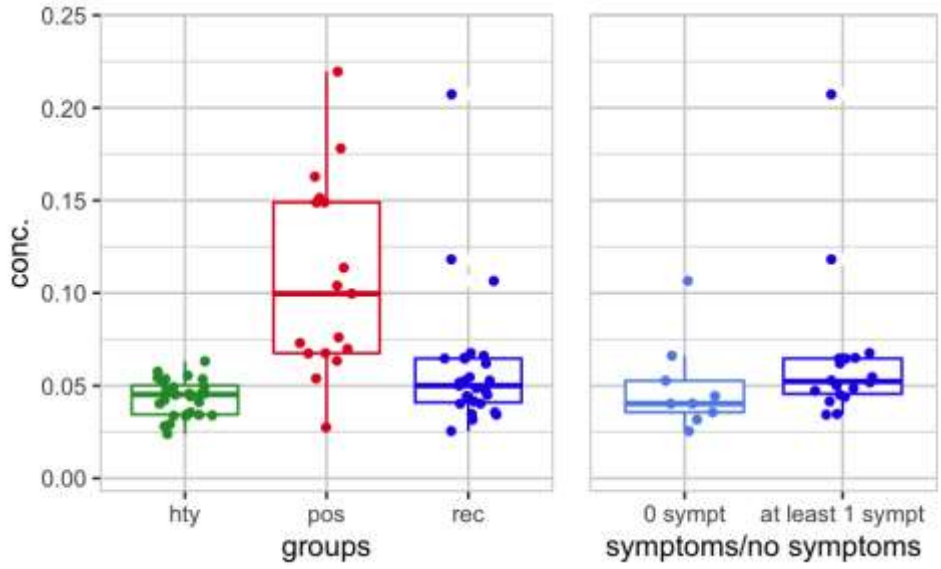


Figure S12: neopterin

targeted MS / pos[17], hty[28], rec[27], total [72]

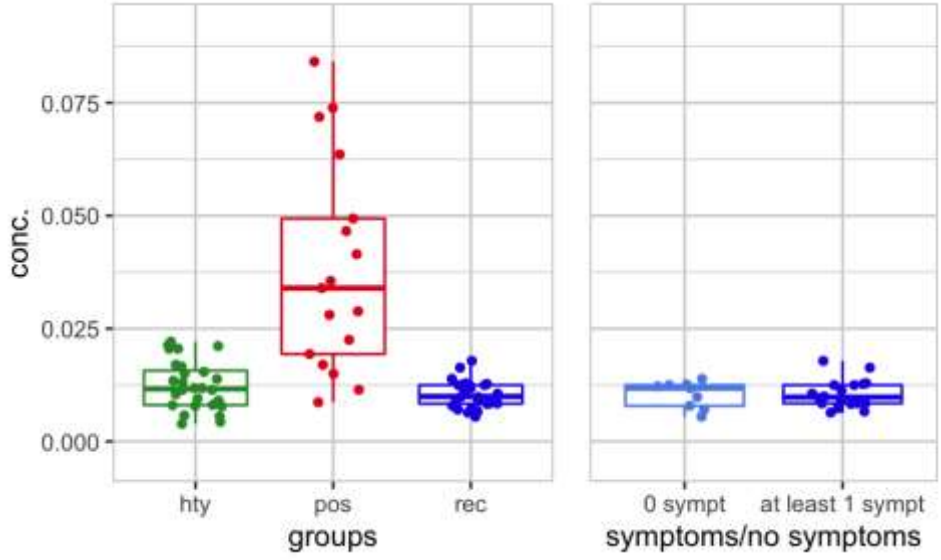


Figure S13: phenylalanine

targeted MS / pos[17], hty[28], rec[27], total [72]

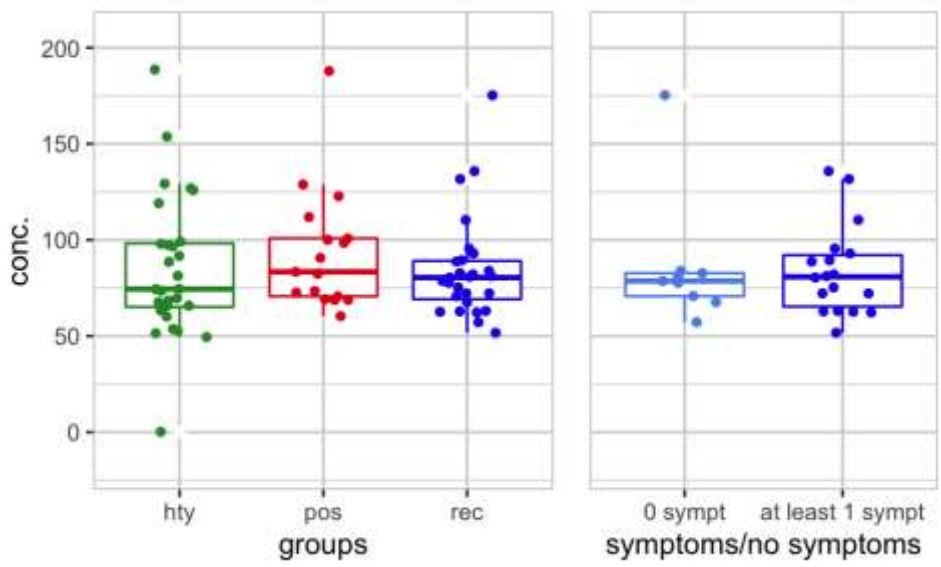


Figure S14: phenylalanine/tyrosine

targeted MS / pos[17], hty[28], rec[27], total [72]

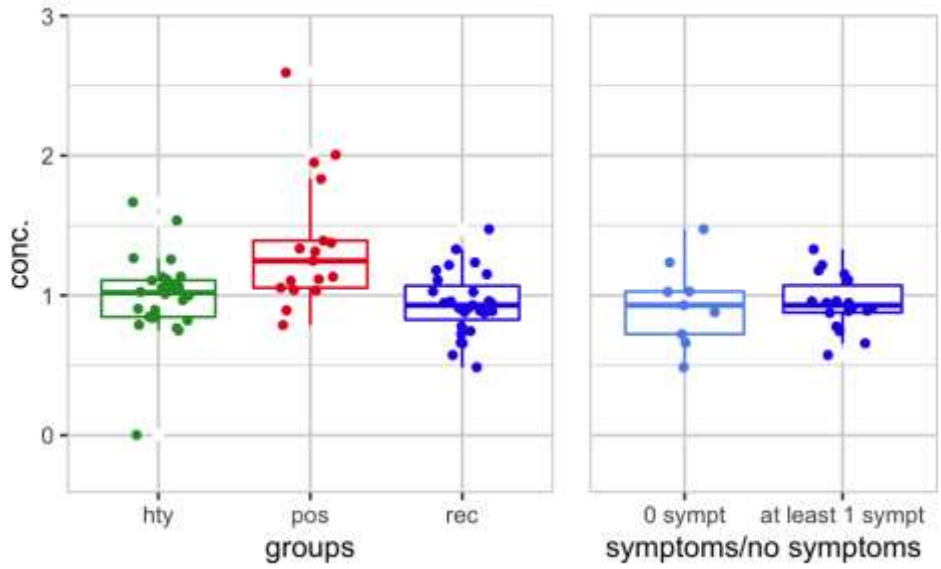


Figure S15: quinolinic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

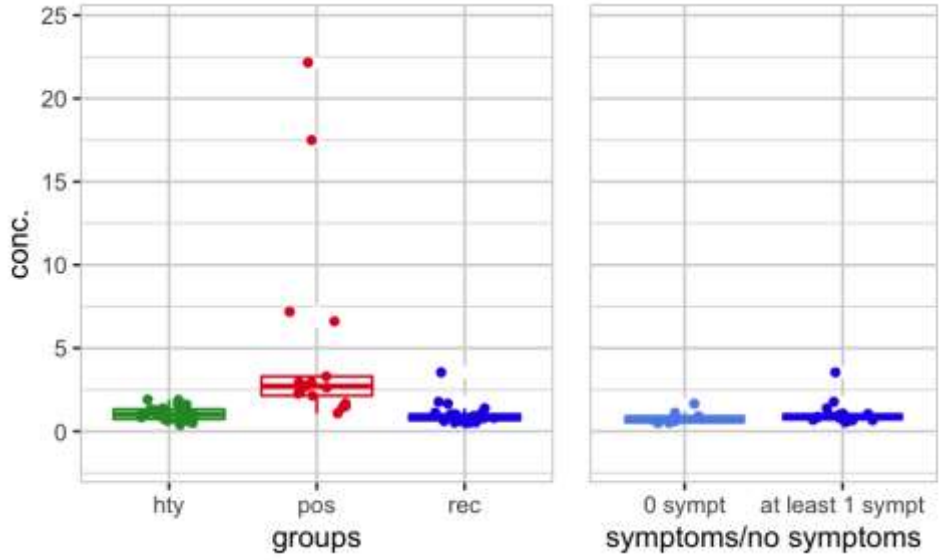


Figure S16: quinolinic acid/kynurenic acid

targeted MS / pos[17], hty[28], rec[27], total [72]

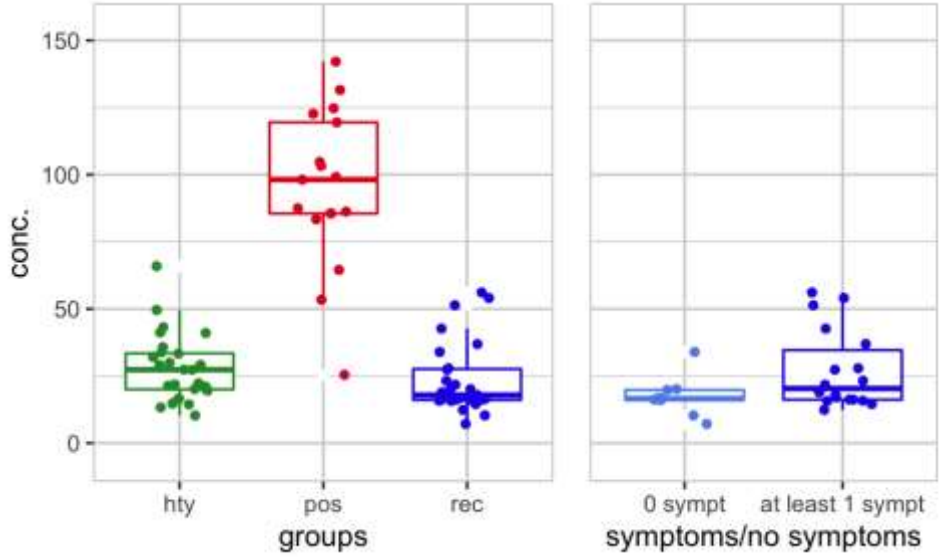


Figure S17: taurine

targeted MS / pos[17], hty[28], rec[27], total [72]

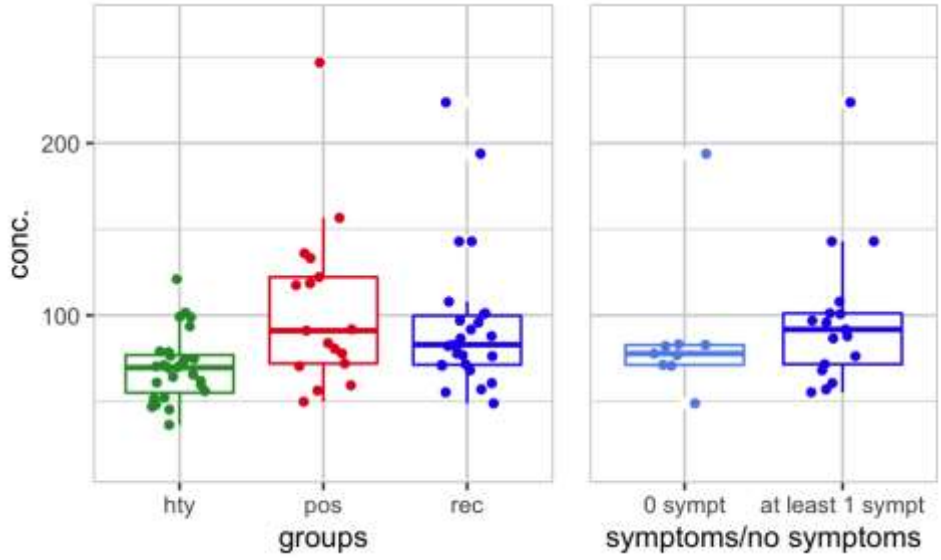
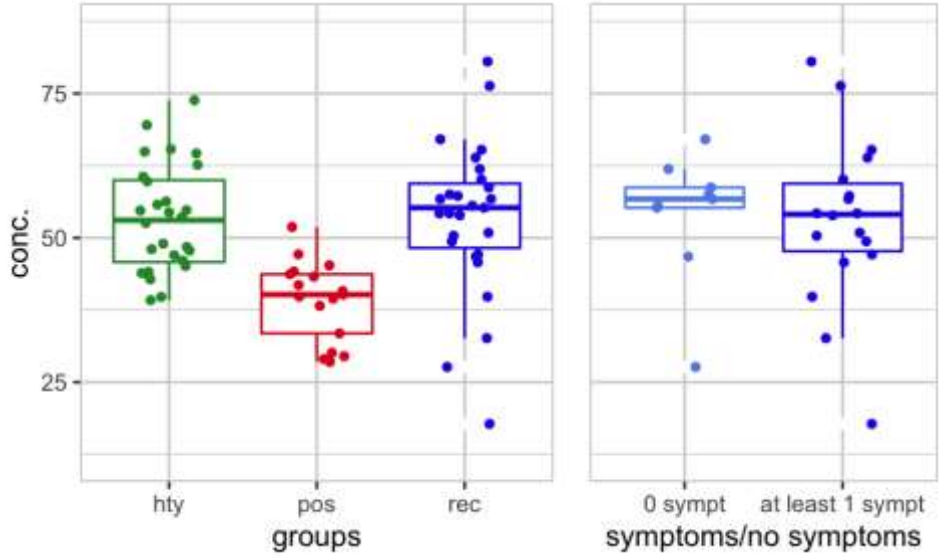


Figure S18: tryptophan

targeted MS / pos[17], hty[28], rec[27], total [72]



Correlations

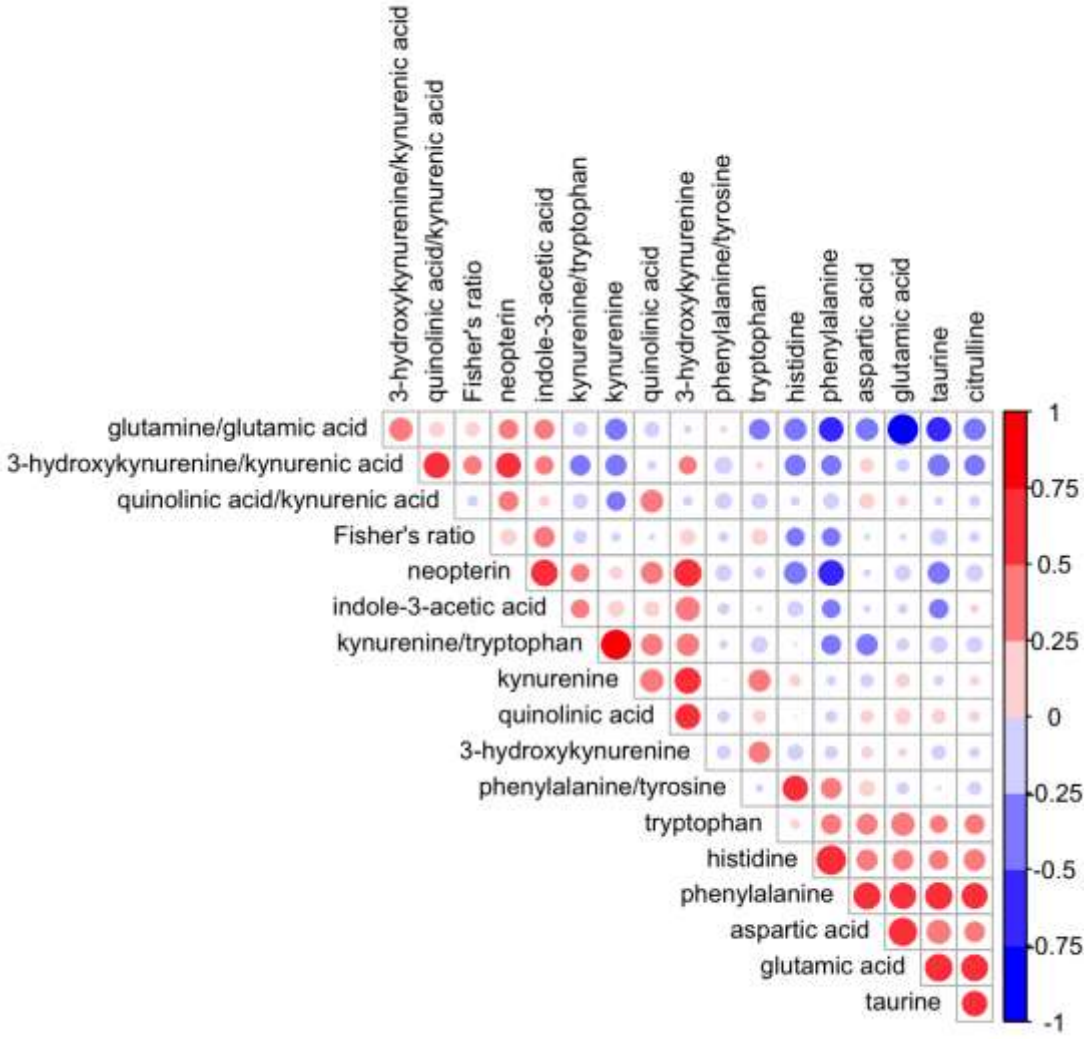


Figure S19: correlation using the healthy population ordered according to hierarchical clustering obtained from healthy control

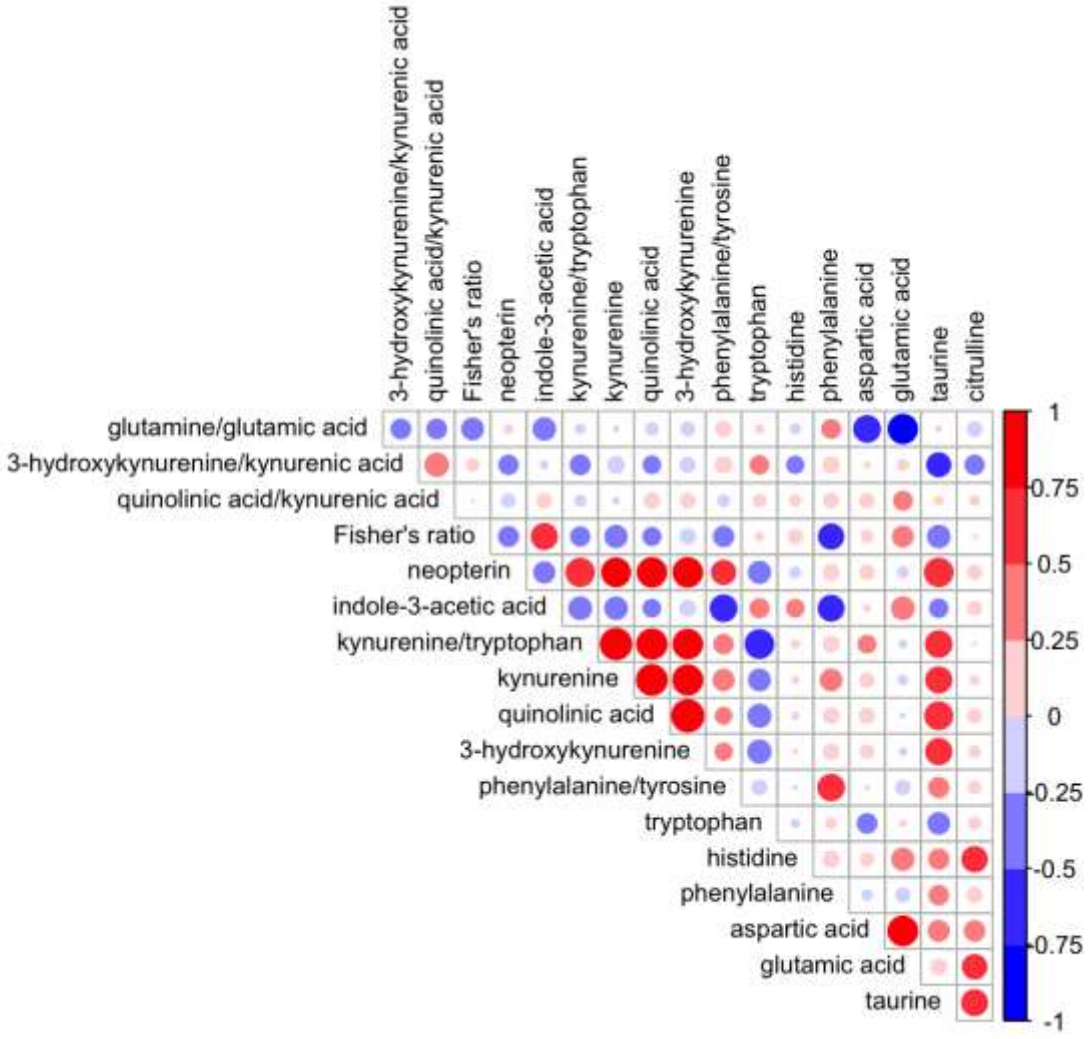


Figure S20: correlation using the positive population ordered according to hierarchical clustering obtained from healthy control

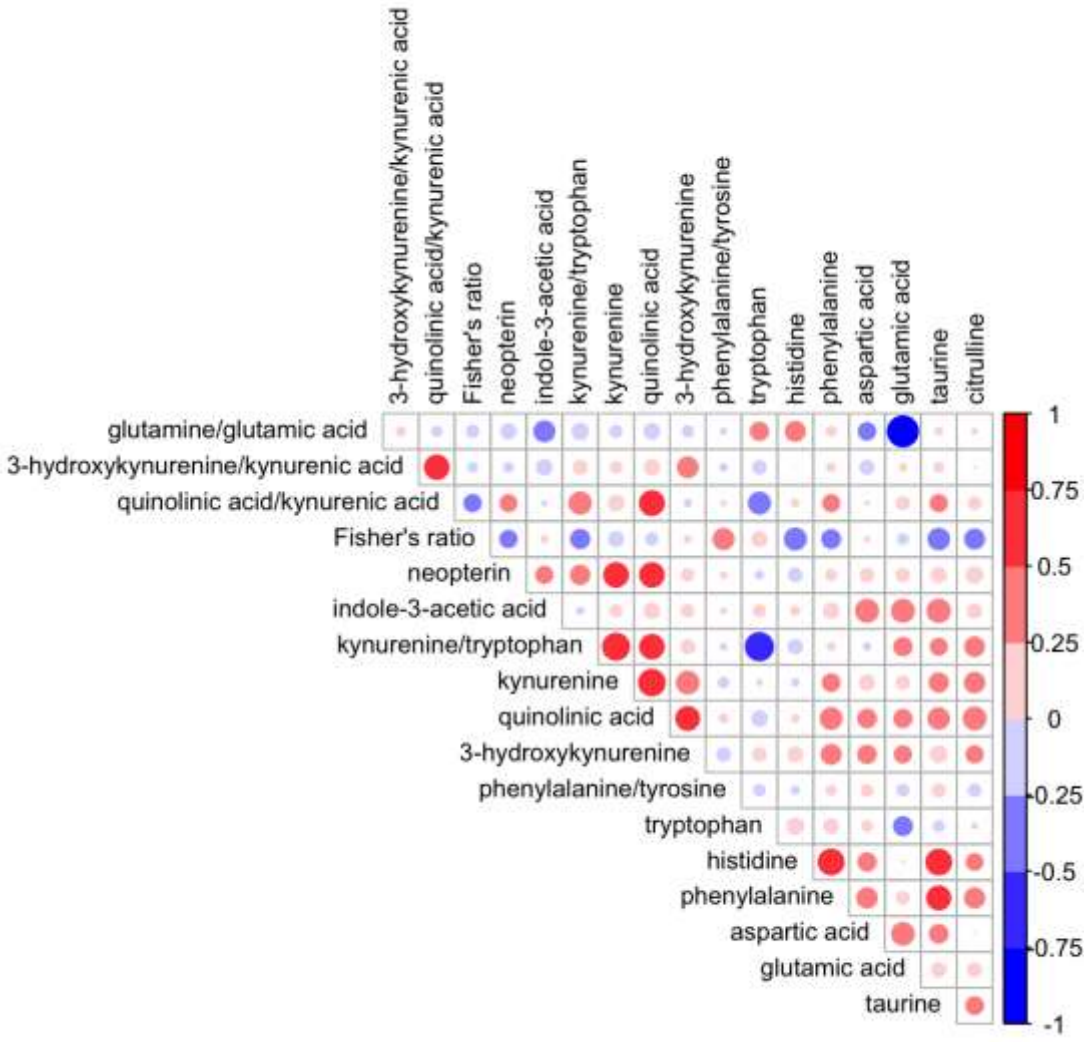


Figure S21: correlation using the recovered population ordered according to hierarchical clustering obtained from healthy control

Lipoproteins measured by IVDR method

Univariate statistics

Figure S22: ABA1

lipoproteins / pos[68], hty[43], rec[27], total [134]

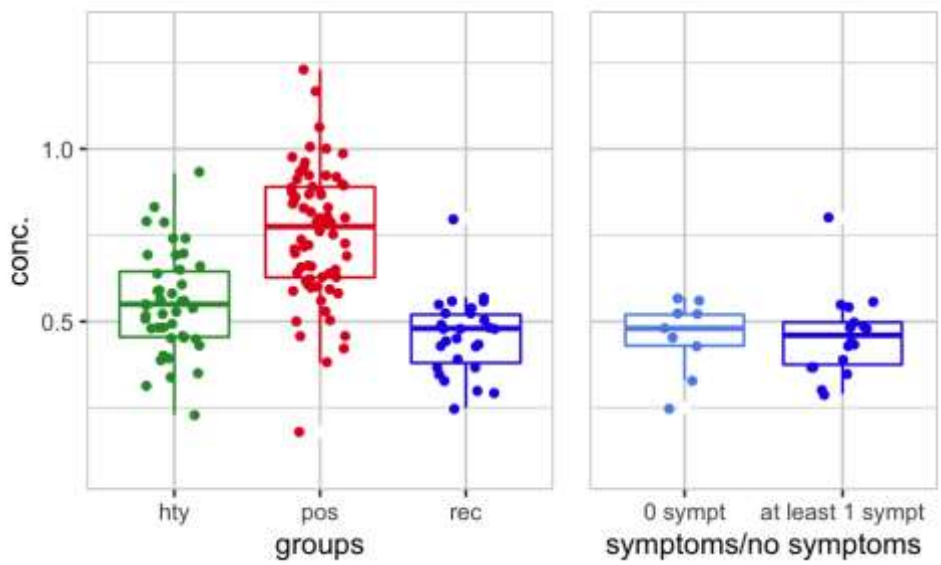


Figure S23: H1FC

lipoproteins / pos[68], hty[43], rec[27], total [134]

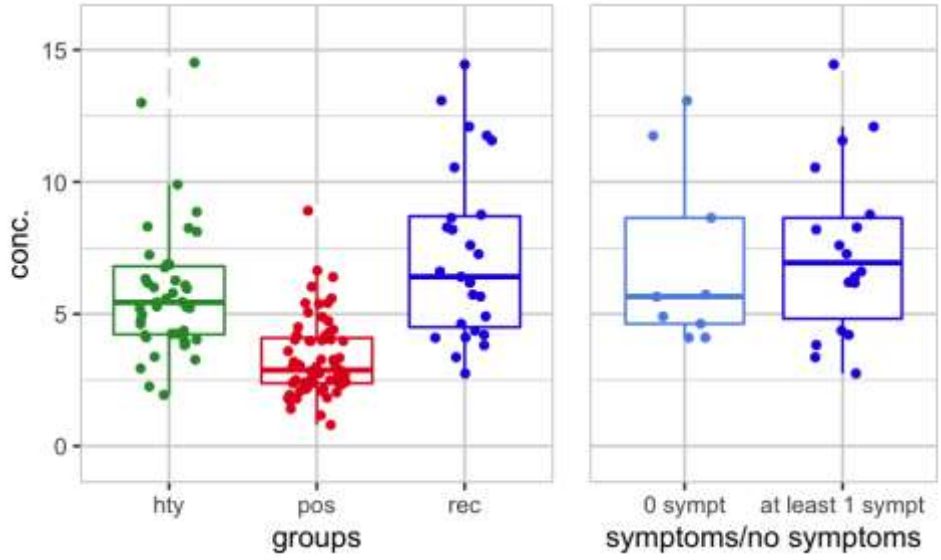


Figure S24: H2A1

lipoproteins / pos[68], hty[43], rec[27], total [134]

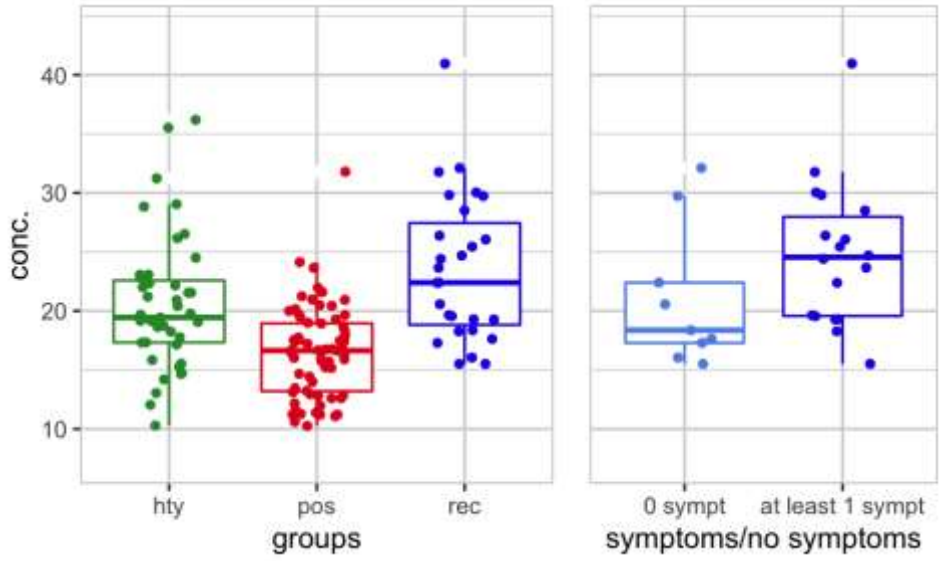


Figure S25: H2FC

lipoproteins / pos[68], hty[43], rec[27], total [134]

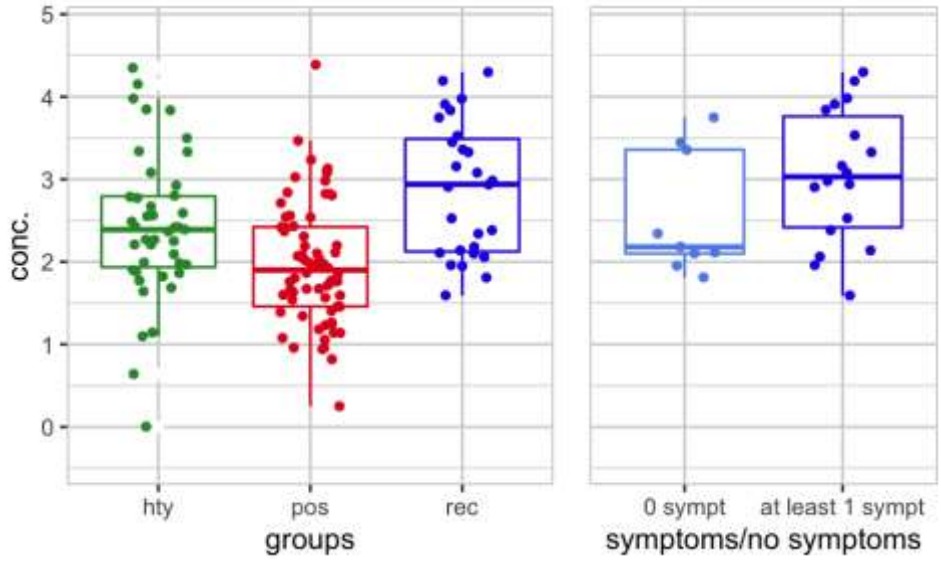


Figure S26: H3A1

lipoproteins / pos[68], hty[43], rec[27], total [134]

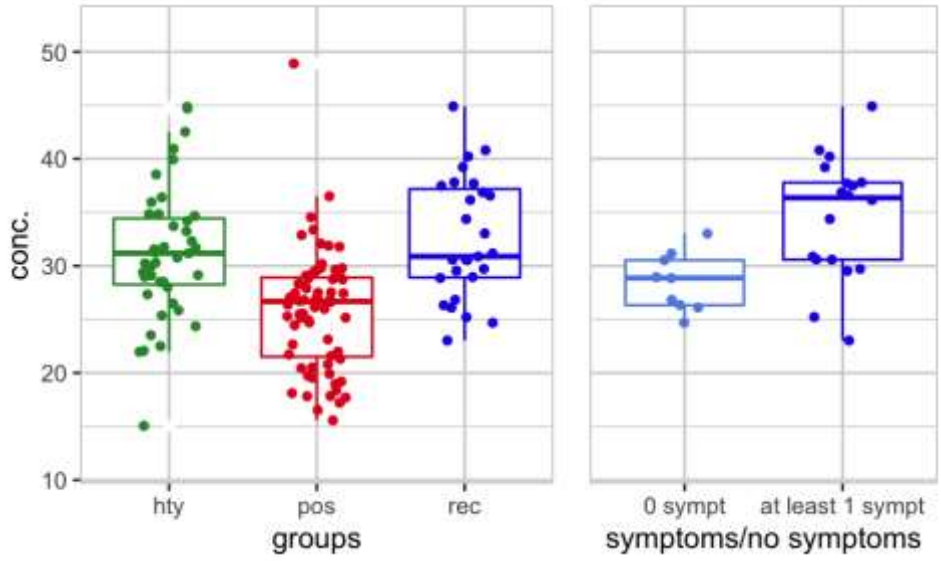


Figure S27: H3CH

lipoproteins / pos[68], hty[43], rec[27], total [134]

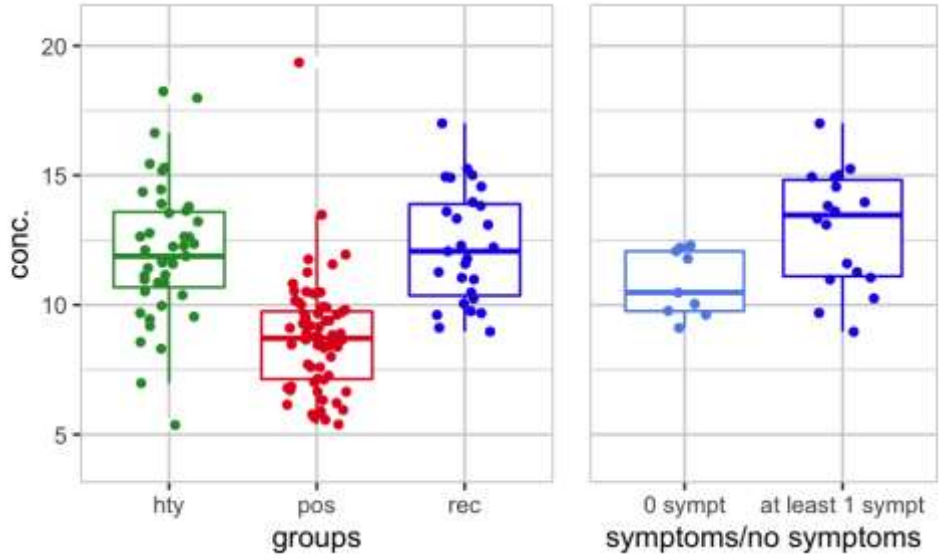


Figure S28: H3FC

lipoproteins / pos[68], hty[43], rec[27], total [134]

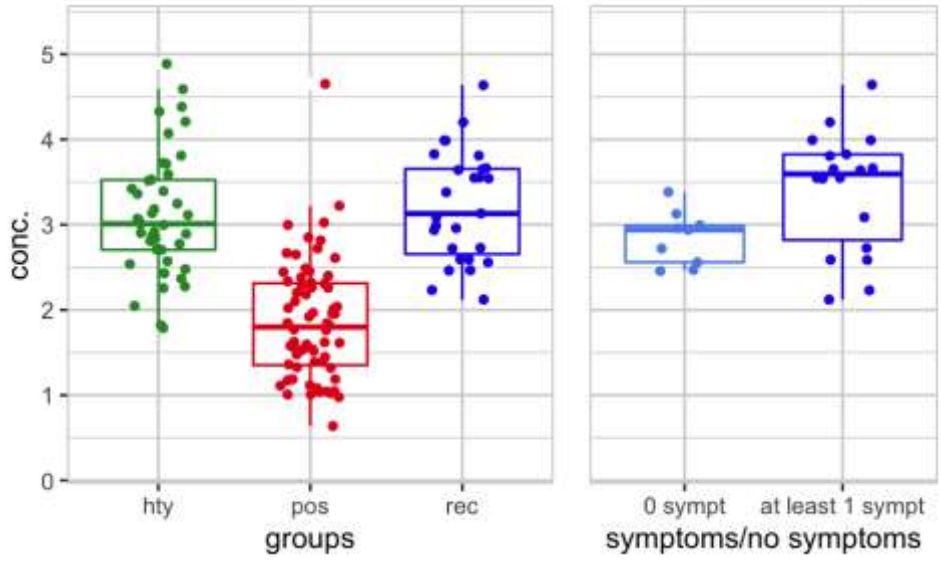


Figure S29: H3PL

lipoproteins / pos[68], hty[43], rec[27], total [134]

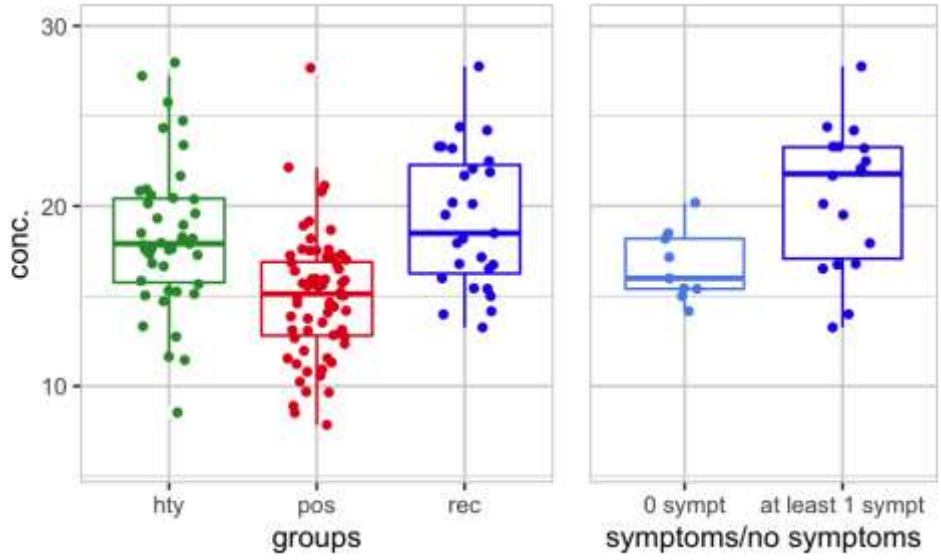


Figure S30: H4A1

lipoproteins / pos[68], hty[43], rec[27], total [134]

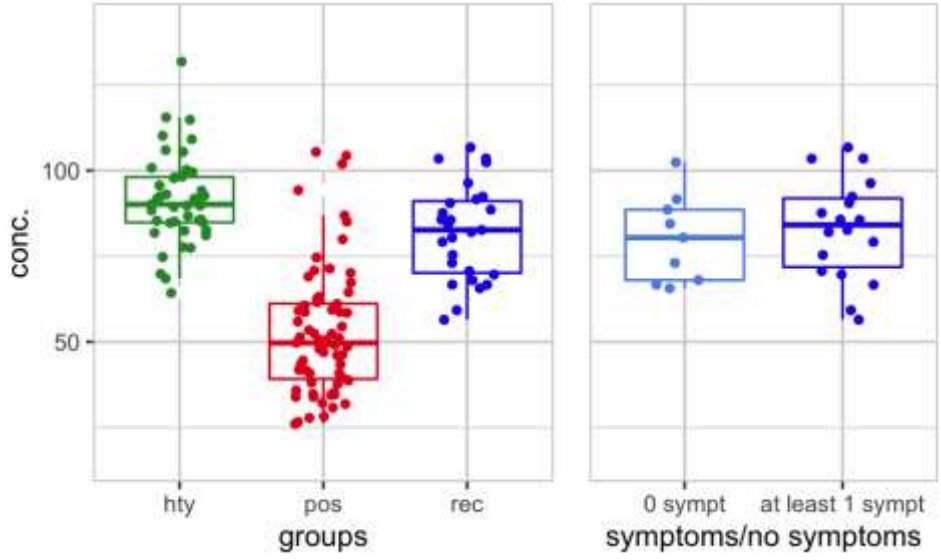


Figure S31: H4A2

lipoproteins / pos[68], hty[43], rec[27], total [134]

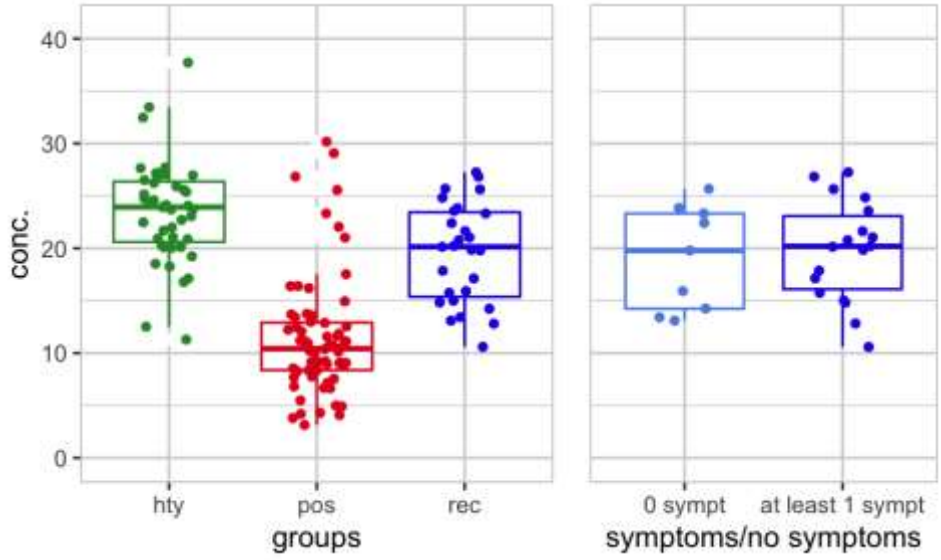


Figure S32: H4CH

lipoproteins / pos[68], hty[43], rec[27], total [134]

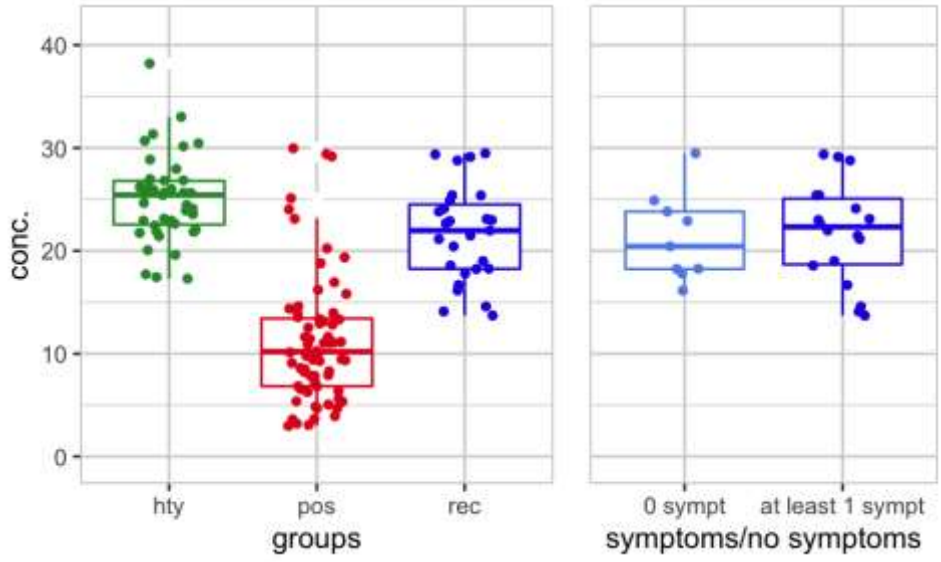


Figure S33: H4FC

lipoproteins / pos[68], hty[43], rec[27], total [134]

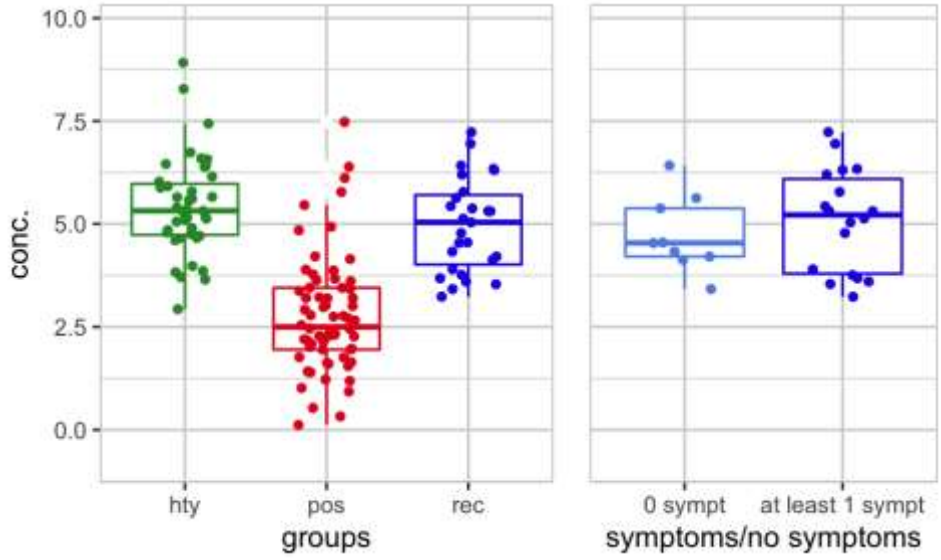


Figure S34: H4PL

lipoproteins / pos[68], hty[43], rec[27], total [134]

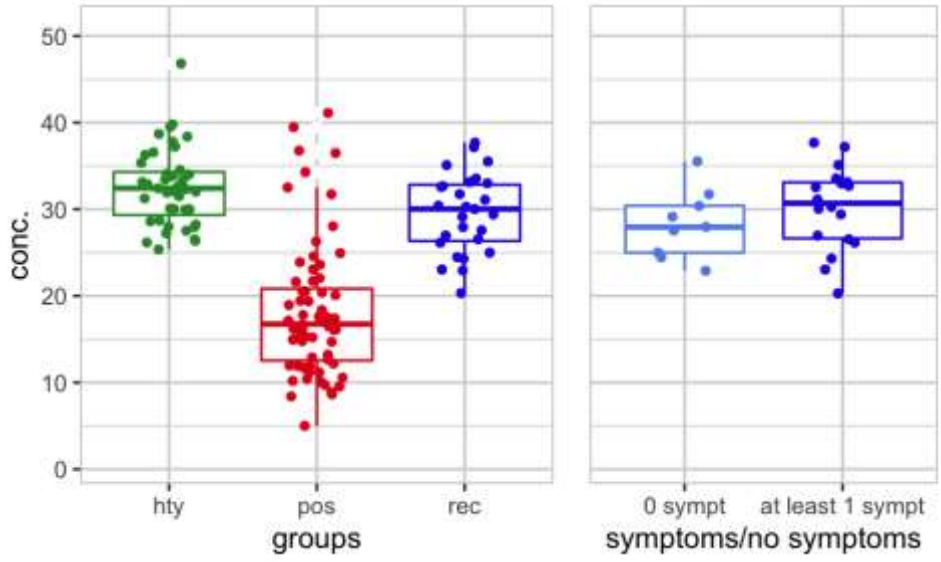


Figure S35: HDA1

lipoproteins / pos[68], hty[43], rec[27], total [134]

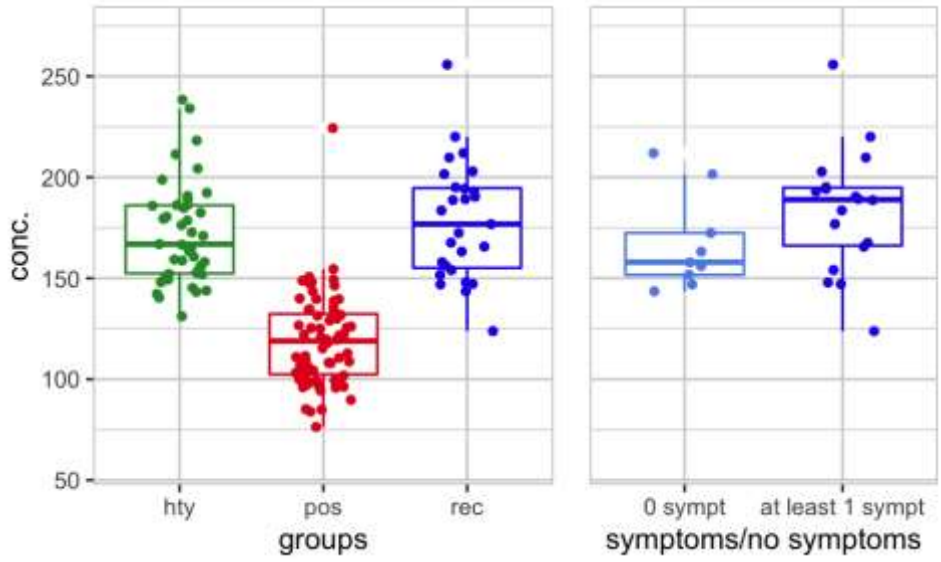


Figure S36: HDA2

lipoproteins / pos[68], hty[43], rec[27], total [134]

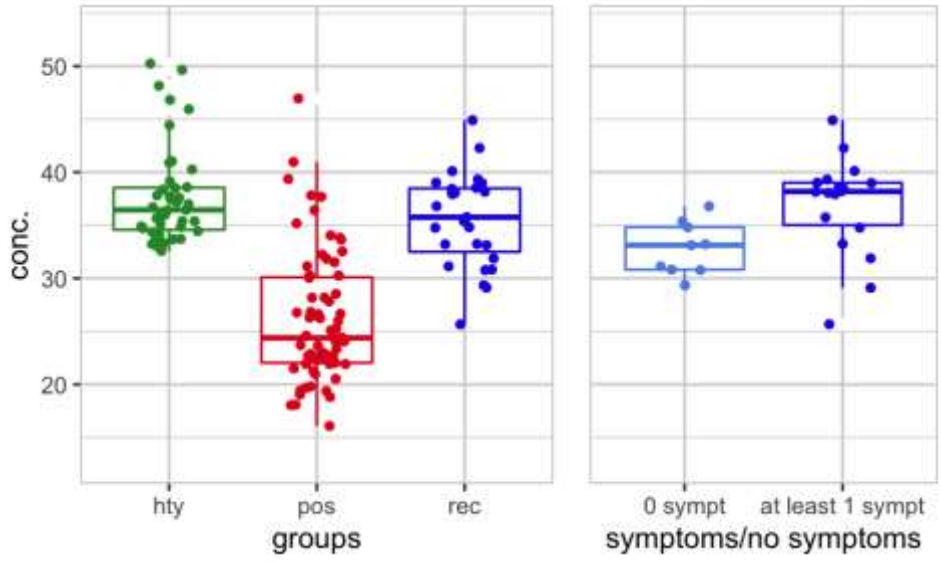


Figure S37: HDCH

lipoproteins / pos[68], hty[43], rec[27], total [134]

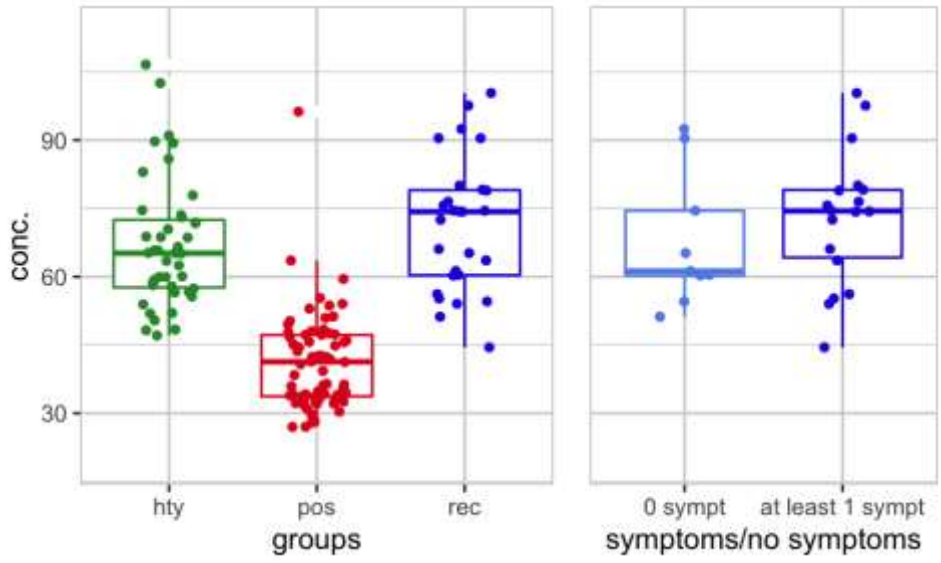


Figure S38: HDFC

lipoproteins / pos[68], hty[43], rec[27], total [134]

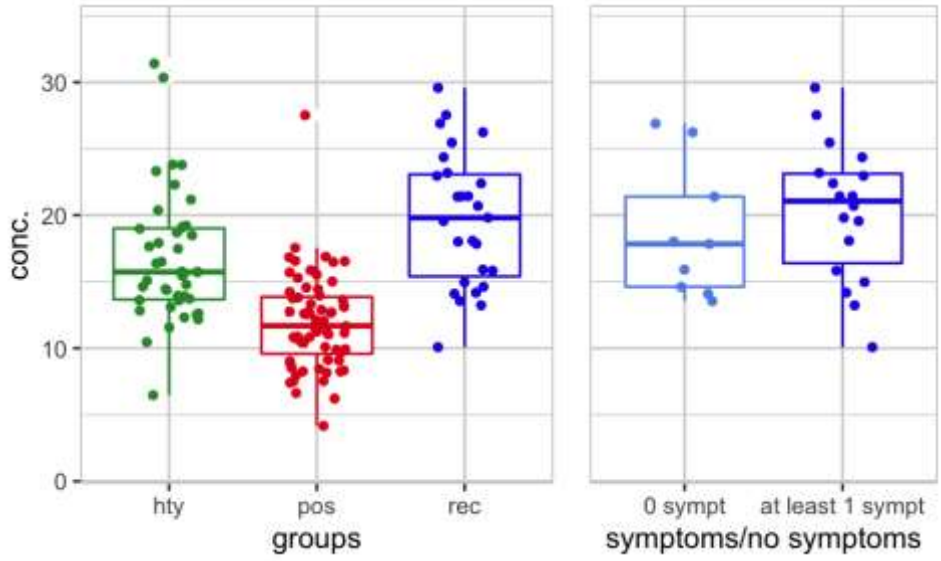


Figure S39: HDPL

lipoproteins / pos[68], hty[43], rec[27], total [134]

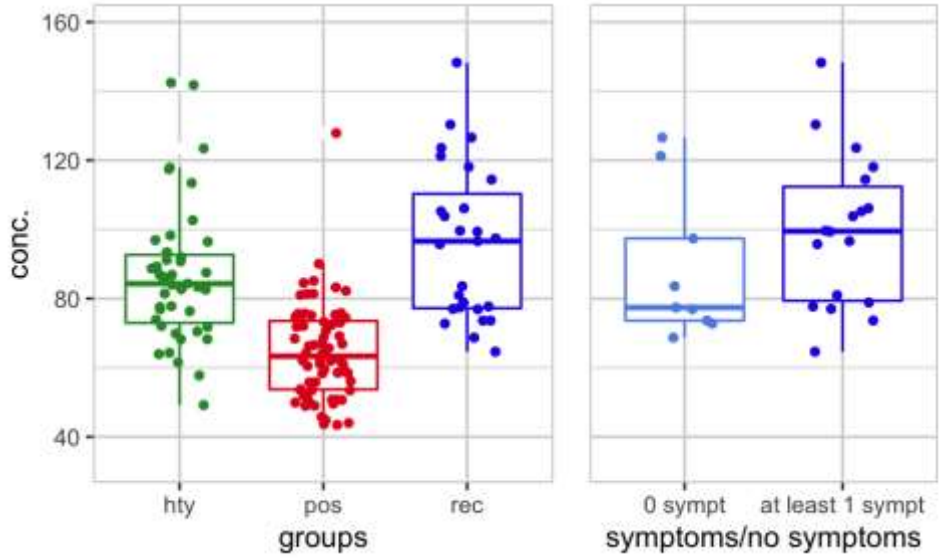


Figure S40: IDAB

lipoproteins / pos[68], hty[43], rec[27], total [134]

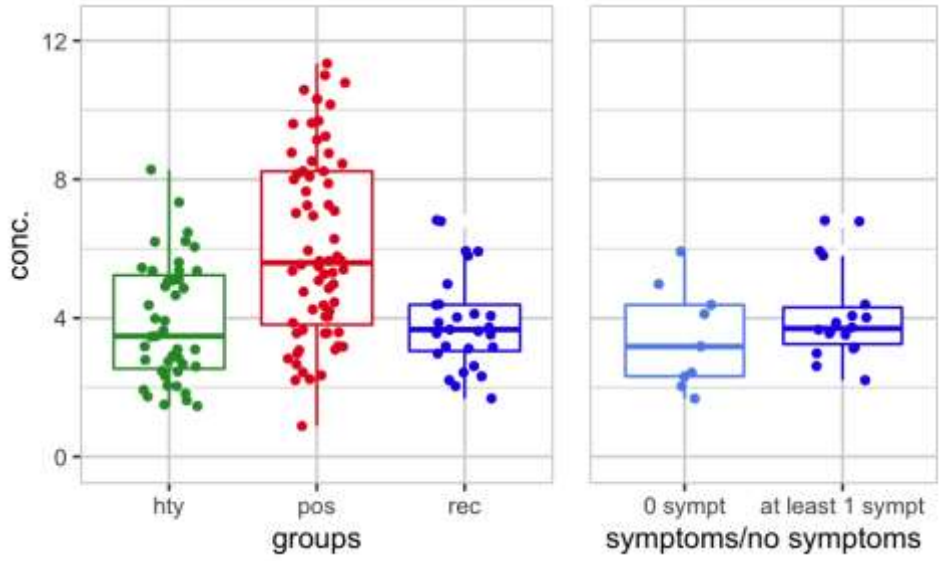


Figure S41: IDPN

lipoproteins / pos[68], hty[43], rec[27], total [134]

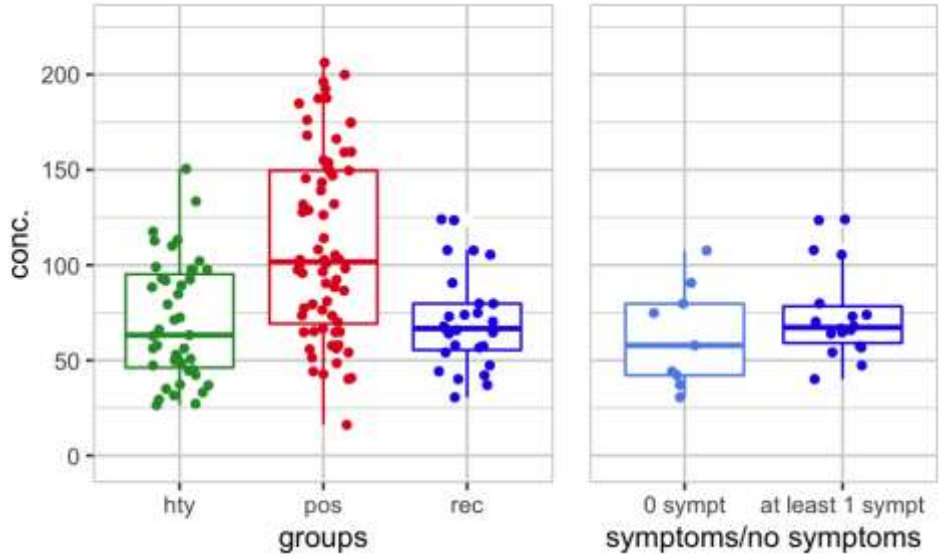


Figure S42: L2TG

lipoproteins / pos[68], hty[43], rec[27], total [134]

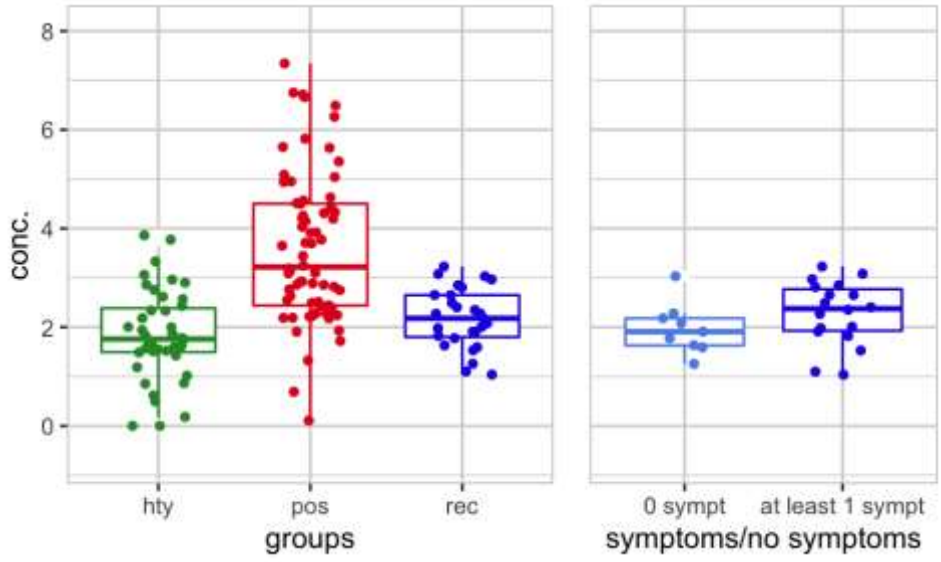


Figure S43: L4TG

lipoproteins / pos[68], hty[43], rec[27], total [134]

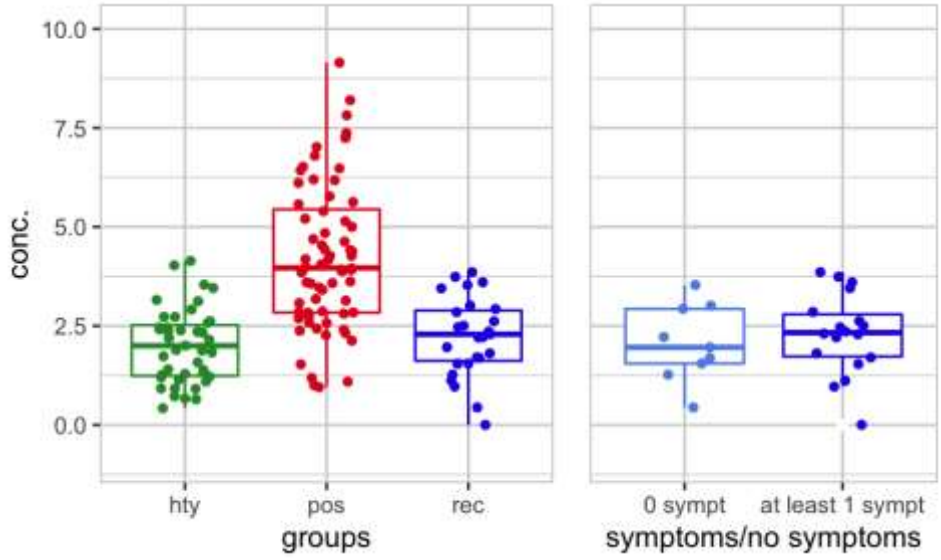


Figure S44: L5TG

lipoproteins / pos[68], hty[43], rec[27], total [134]

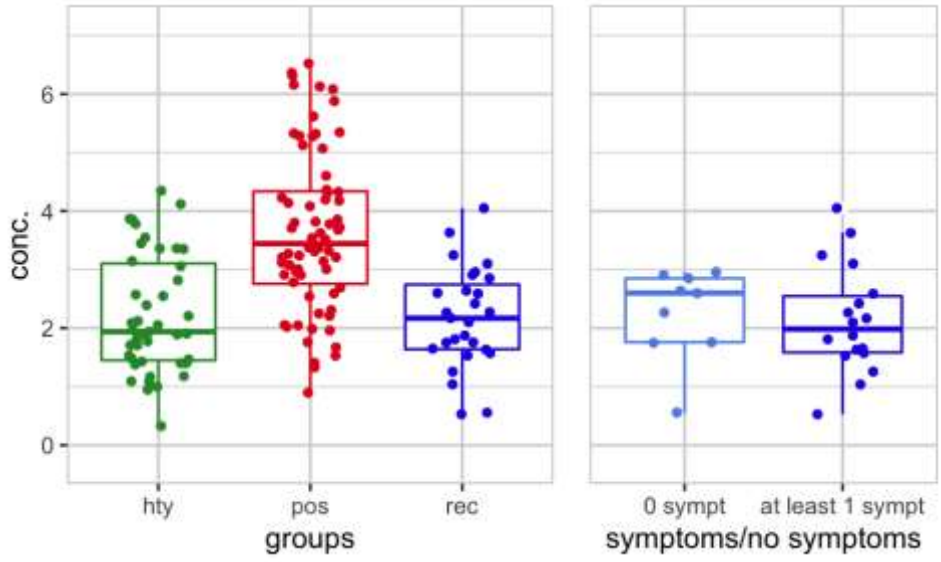


Figure S45: LDHD

lipoproteins / pos[68], hty[43], rec[27], total [134]

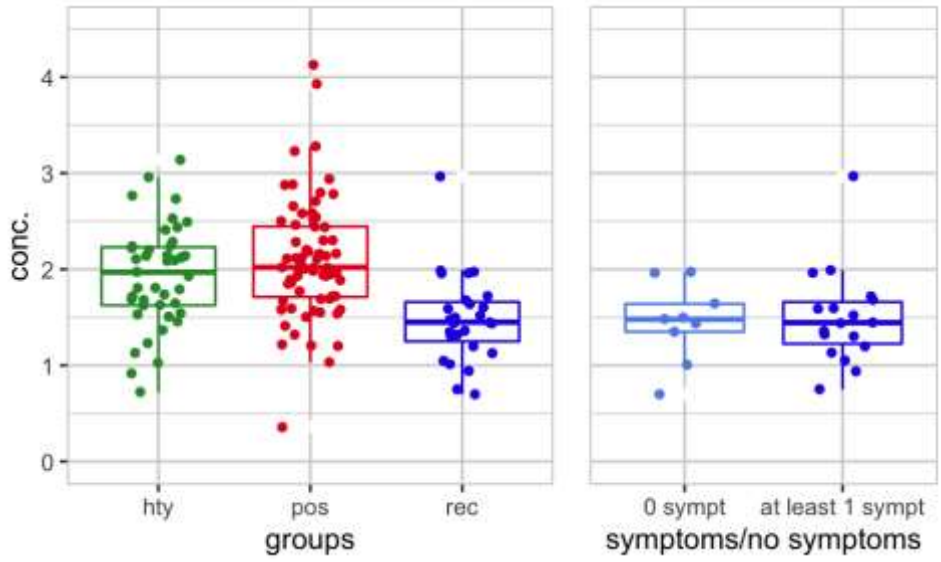


Figure S46: LDTG

lipoproteins / pos[68], hty[43], rec[27], total [134]

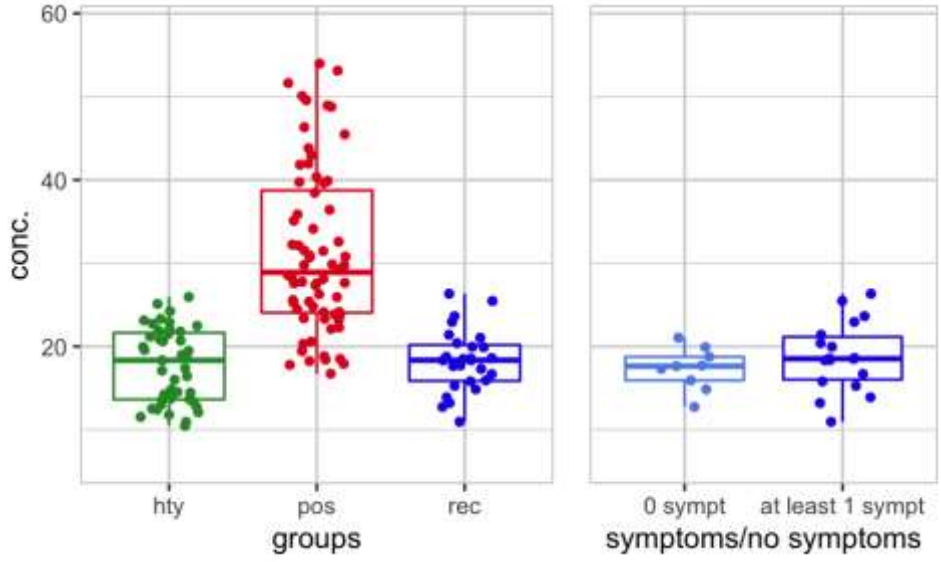


Figure S47: TPA1

lipoproteins / pos[68], hty[43], rec[27], total [134]

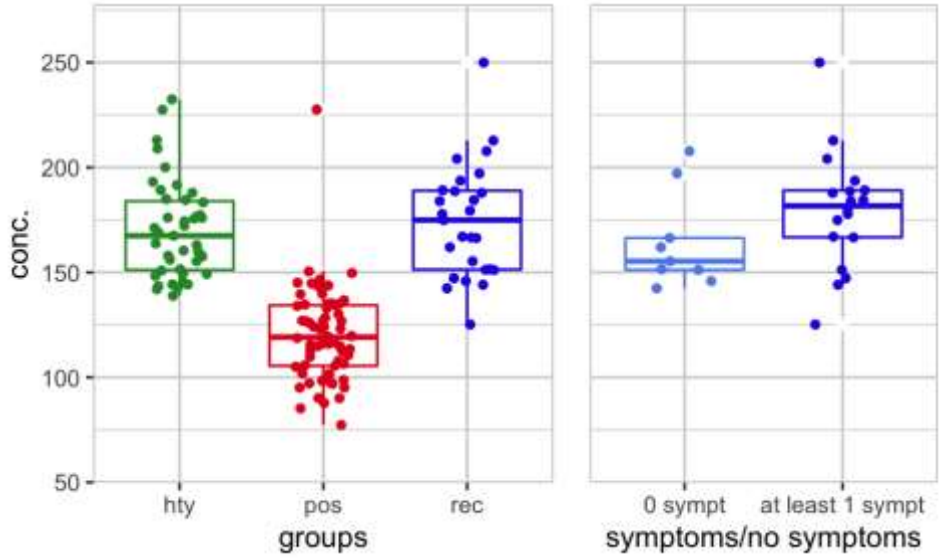


Figure S48: TPA2

lipoproteins / pos[68], hty[43], rec[27], total [134]

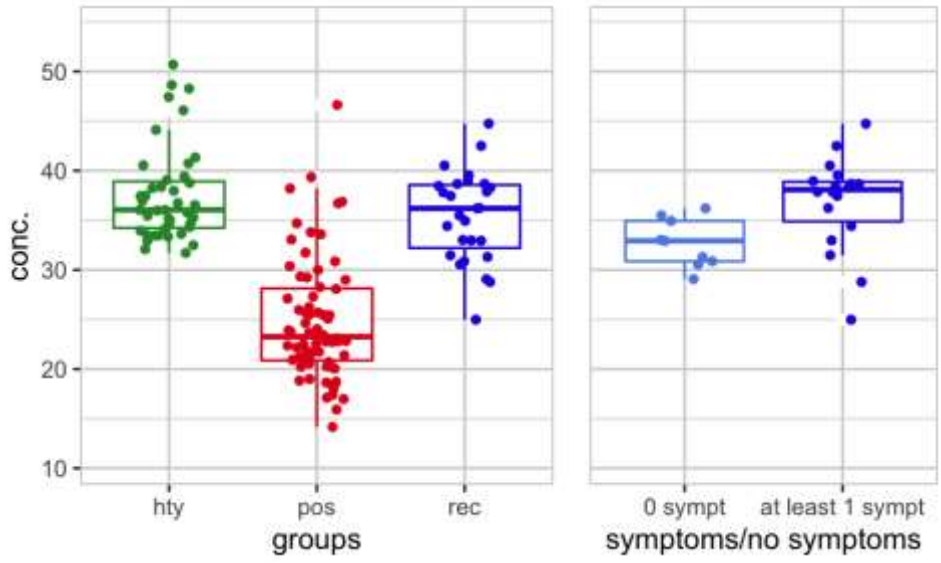


Figure S49: TPCH

lipoproteins / pos[68], hty[43], rec[27], total [134]

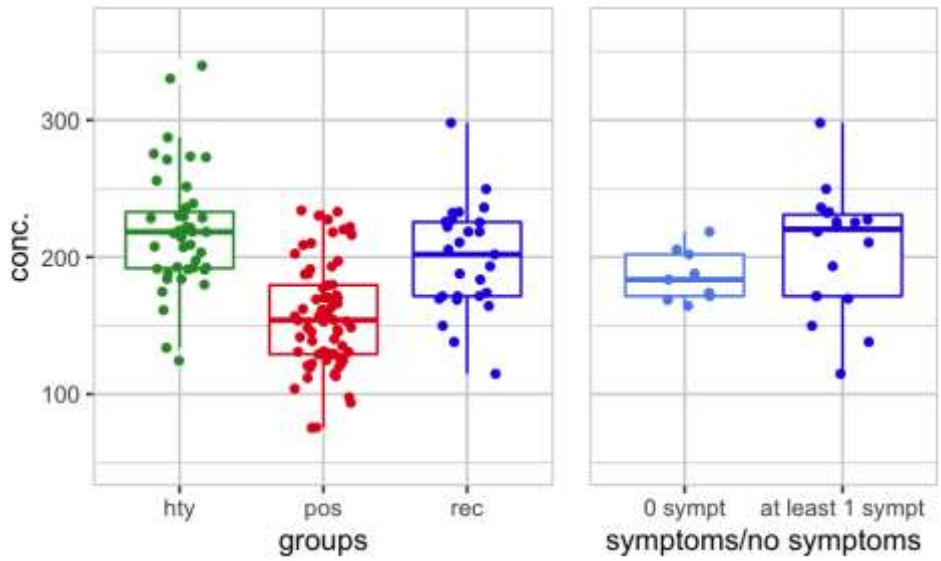
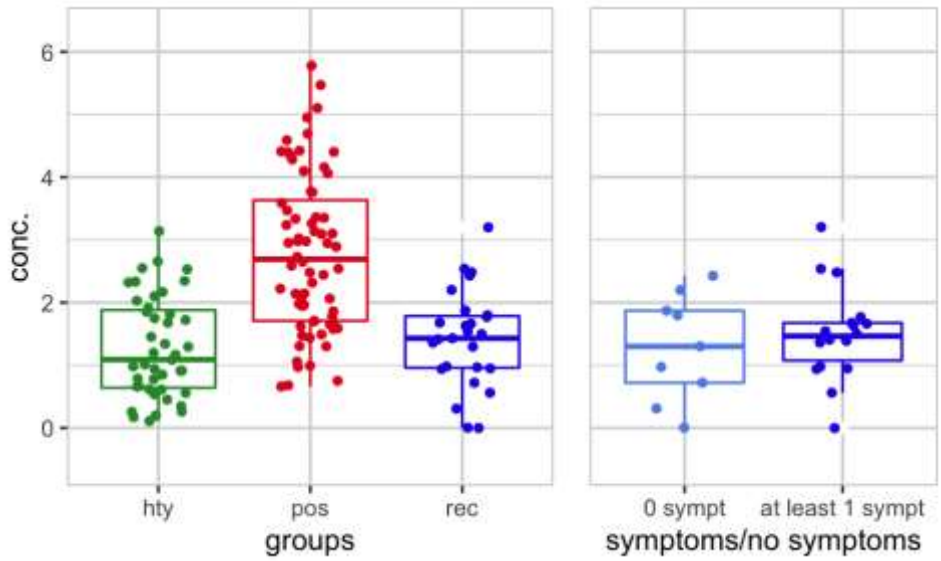


Figure S50: V4FC

lipoproteins / pos[68], hty[43], rec[27], total [134]



correlation matrix

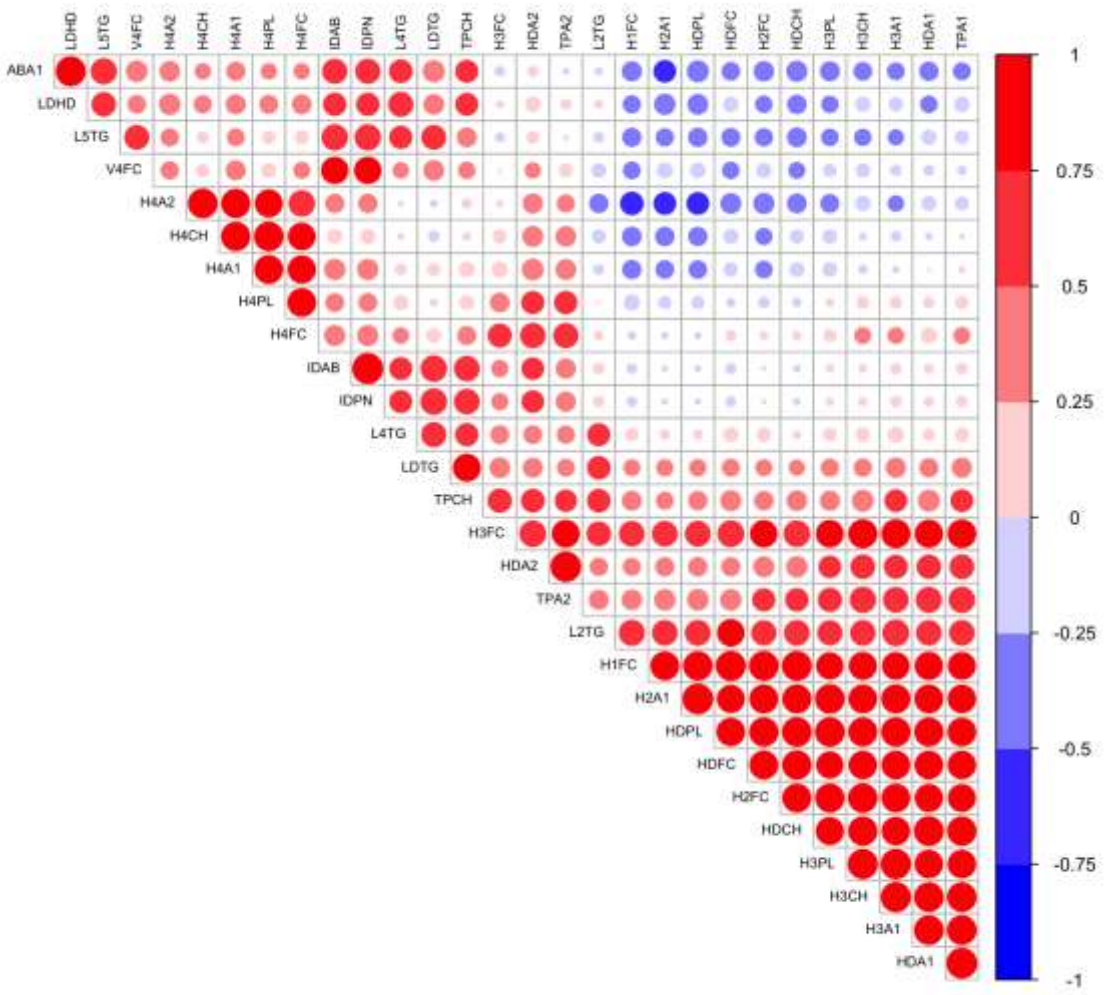


Figure S51: correlation using the healthy population ordered according to hierarchical clustering

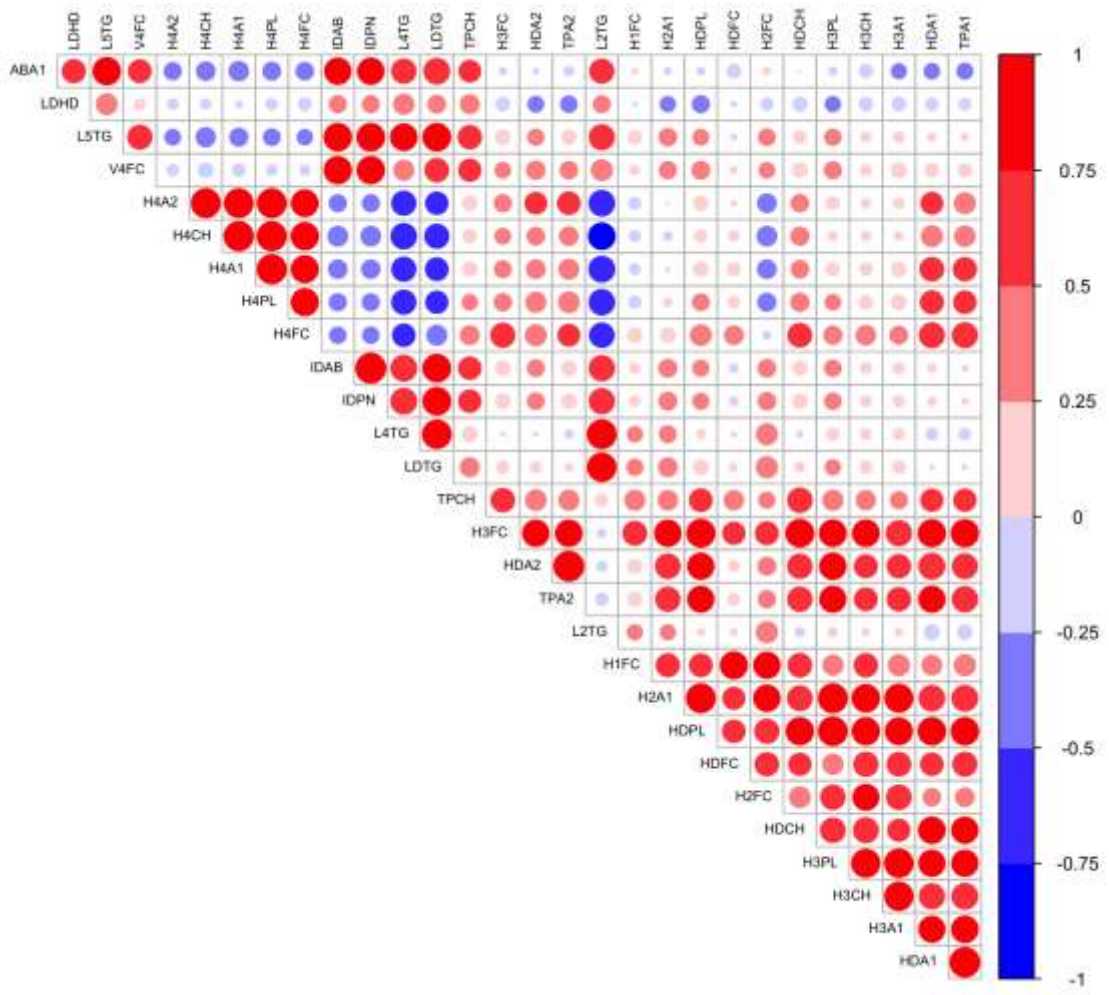


Figure S52: correlation using the positive population ordered according to hierarchical clustering obtained from healthy control

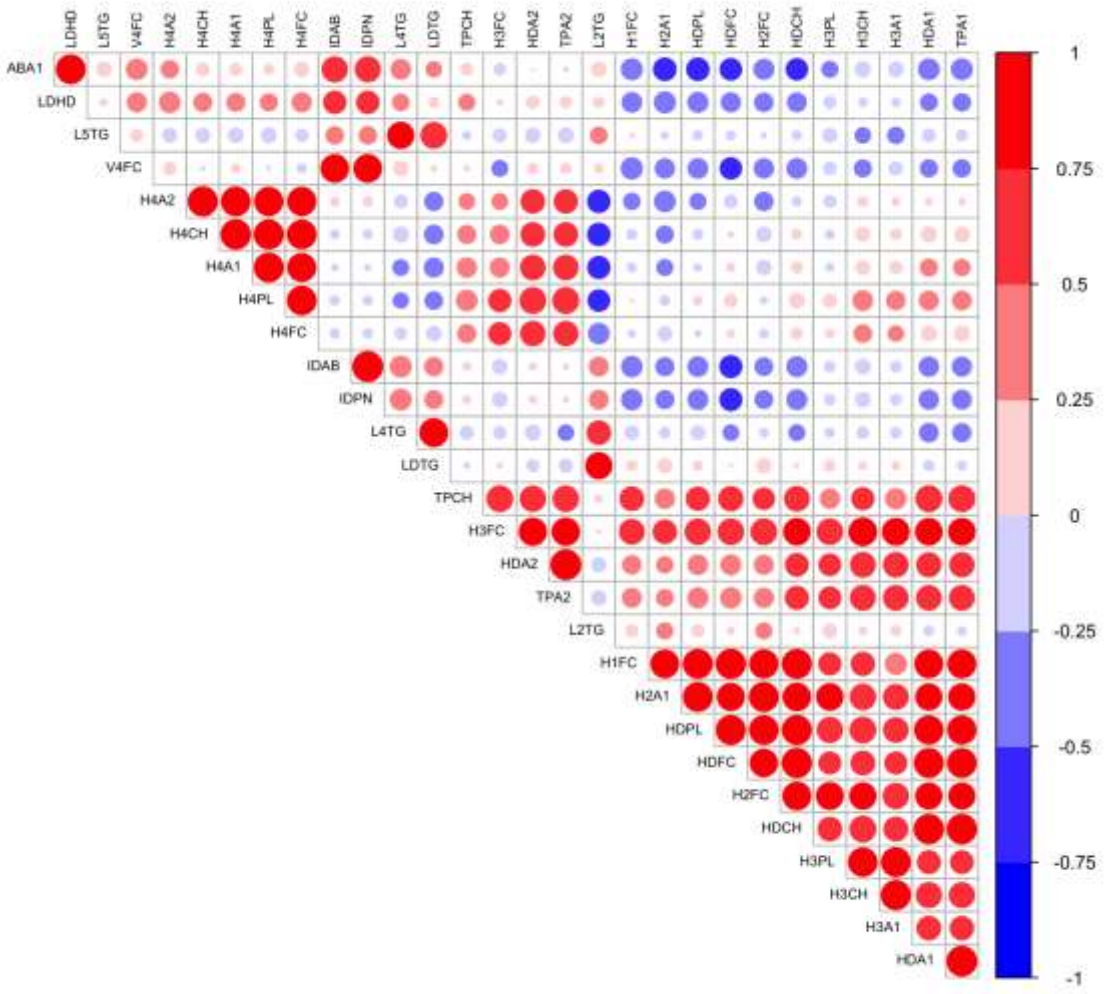


Figure S53: correlation using the recovered population ordered according to hierarchical clustering obtained from healthy control

Small molecules measured by IVDR method

Here we report the concentrations of small molecules measured from nmr spectra.

univariate statistics

pos[68], hty[43], rec[27], total [138]

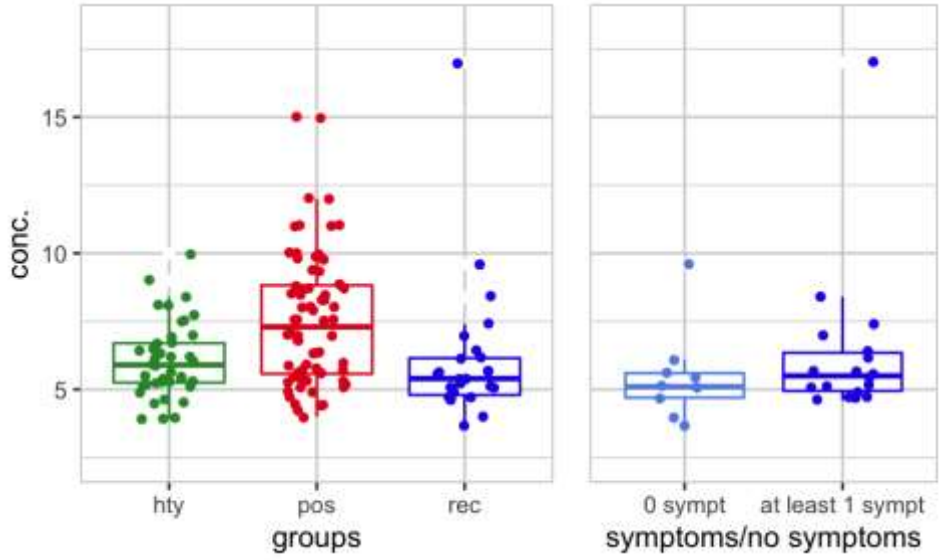


Figure S54: Glucose

Diffusion and Relaxation edited NMR experiments

Univariate statistics

Integrals measured from DIRE experiments.

Figure S55: GlycA

NMR integrals / pos[57], hty[34], rec[31], total [122]

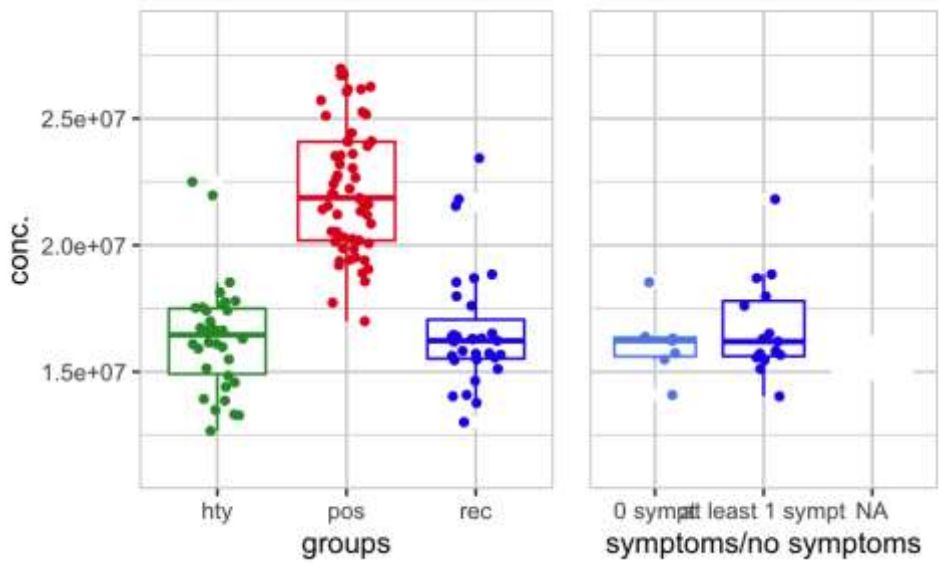


Figure S56: GlycB

NMR integrals / pos[57], hty[34], rec[31], total [122]

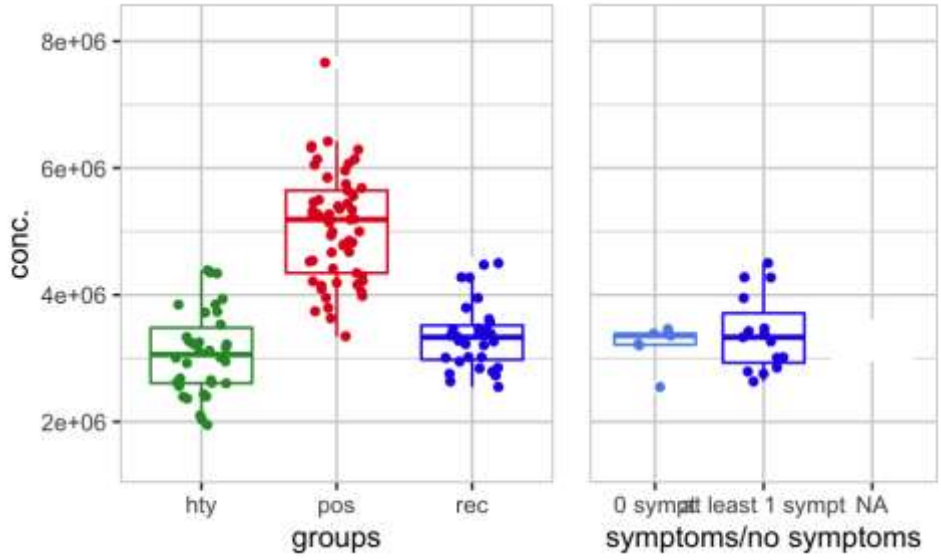


Figure S57: Spc Total

NMR integrals / pos[57], hty[34], rec[31], total [122]

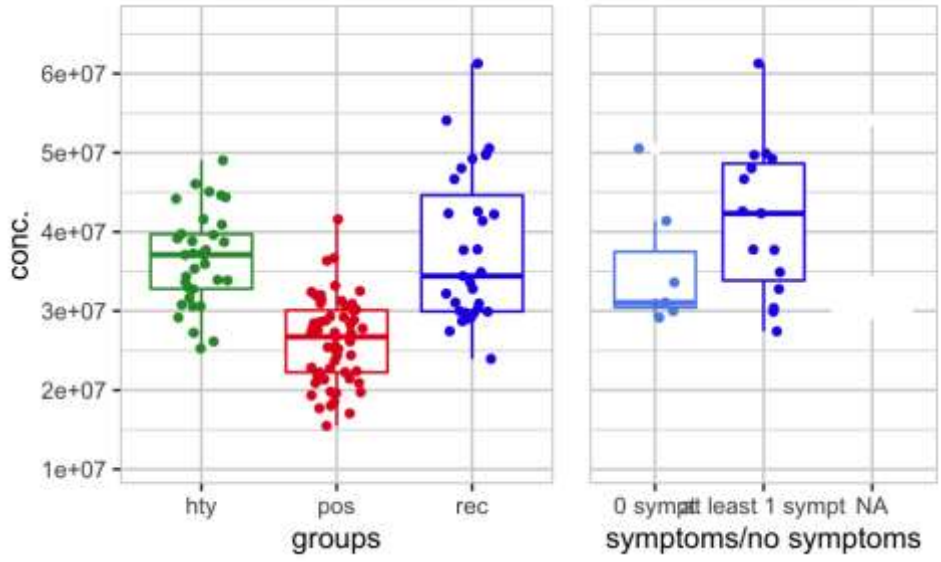


Figure S58: Spc Total / GlycA

NMR integrals / pos[57], hty[34], rec[31], total [122]